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**ANNIVERSARIES**

Congratulations on the 55-years-old anniversary of Professor S.V. Ziablitsev

## OZONETHERAPY INFLUENCE ON MORPHOLOGIC CHANGES OF LIVER IN PURULENT INFLAMMATION OF THE LUNGS IN THE EXPERIMENT

<sup>1</sup>Alyavi A.L., <sup>1</sup>Sadykova G.A., <sup>1</sup>Rakhmatullaev Kh.U., <sup>1</sup>Tadjikhodjaeva Yu. Kh., <sup>2</sup>Zalyalova Z.S.

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**Relevance.** Ozone increases the oxygen transport function of the blood. The use of ozone therapy for pulmonary pathology is promising. The effect of ozone therapy is associated with the ability of ozone to eliminate hypoxemia and tissue hypoxia, which is always present in patients with pathology of the bronchopulmonary apparatus.

**Objective:** to study morphofunctional changes in liver tissue, in the dynamics of the use of ozonized water in rats in an experimental model of chronic purulent pneumonia.

**Materials and methods.** Three groups were formed from 30 male white rats (180-200 g). In group 1 (n = 10) healthy rats were injected intraperitoneally with 5 ml of ozonated (0.02 mg / L) 0.9% NaCl once a day for 10 minutes. Course 10 days. Animals of the 2 (n = 10) and 3 (n = 10) groups were first modeled for chronic pneumonia. For this, under local novocaine anesthesia, a 1.5-2.0 cm long incision was made on the animal's neck. A nylon thread with a diameter of 0.4 mm and a length of 10-12 cm was inserted into the lumen of the trachea, between its rings, on a thin piercing needle. The distal end of the thread was located in the lumen of the trachea, and its proximal end was fixed on the skin. The wound was sutured tightly in layers. After 45 days, the thread was removed without opening the trachea. Subsequently, animals of group 2 did not receive treatment. And rats of group 3 were injected once a day with 5 ml of ozonized (0.02 mg / l) 0.9% NaCl for 10 minutes. Course 10 days. The animals were removed from the experiment by instant decapitation. The taken pieces of the liver were fixed in formalin. Histological sections were stained with hematoxylin and eosin. Microscopy was performed using an XS-213 light microscope and a Leica microscope.

**Results.** With prolonged irritation of the respiratory tract, structural changes in the liver, characteristic of toxic hepatitis, were revealed. After treatment with ozonated saline, the morphological picture of the liver improved. In healthy rats, ozone therapy did not have a negative effect on the general condition and behavior of the animals.

**Conclusions.** Treatment with ozonated saline improves the morphological picture of the liver of rats with chronic pneumonia.

**Keywords:** chronic purulent inflammation of the lungs, rats, ozone therapy, morphology, liver.

**Relevance.** Maintaining immune homeostasis of the lungs depends on a balance of sufficiently effective defense mechanisms that ensure the elimination of inhaled pathogens, and equally effective mechanisms of inhibiting inflammation to limit subsequent damage to lung tissue. Chronic inflammation of the respiratory system occupies a significant proportion among diseases in general [1, 8, 11]. The effect of ozone therapy is determined by the high oxidation-reduction potential of ozone, which provides a dual mechanism of action (in therapeutic doses). The first one is local, with disinfecting activity against bacteria, viruses and fungi. The second is systemic, metabolic in relation to protein-lipid complexes of plasma and cell membranes, leading to an increase in oxygen tension, transformation and synthesis of biologically active substances, increased activity of immunocompetent cells, improved rheology and oxygen transport function of blood [6]. At the same time, unlike many antiseptics, ozone does not have a destructive and irritating effect on tissues [3, 7]. The use of ozone for the treatment of a number of diseases is pathogenetically justified [1, 7, 9]. Ozone acts simultaneously on several links in the pathogenesis of many diseases.

There is a favorable effect of ozonized saline solution on the liver in experimental peritoneal inflammation, which is manifested in the maintenance of plastic and energy homeostasis of hepatocytes. Good clinical results are observed when ozone is used as a treatment for chronic diffuse liver diseases, including viral etiology. The combination of ozone therapy procedures with interferon made it possible to achieve good clinical results: the state of health improved in most patients, weakness, heaviness and pain in the liver area disappeared. Normalization of disturbed biochemical parameters was noted [4].

There is some opinion, that when using high concentrations of ozonized physiological solution, it is necessary to use vitamin E. The most effective is 5 ozone therapy procedures, which is associated with the rapid stabilization of the process of lipid peroxidation (LPO) [6]. It is shown that during artificial circulation ozone increases the oxygen transport function of the blood, improving the state of the microcirculatory bed of organs, enhances the release of oxygen to tissues and thereby prevents the development of hypoxia. In particular, the liver maintains a normal content of glucose, glycogen, glucose-6-phosphate and pyruvate, the degree of severity

of degenerative changes in hepatocytes decreases. Under the influence of ozone, structural and functional mechanisms are stimulated in liver cells that convert fatty energy substrates into carbohydrate ones, which are easier to use in extreme and pathological conditions. This decreases the likelihood of both the development of fatty dystrophy, as well as the formation of toxic ketone products from fatty acids [4].

The use of ozone therapy for pulmonary pathology is promising. The effect of ozone therapy is associated primarily with the ability of ozone to eliminate hypoxemia and tissue hypoxia, which is always present in patients with pathology of the bronchopulmonary apparatus due to the presence of respiratory failure of varying severity. The complex morpho-functional organization of the lungs, as a polyfunctional organ responsible for the regulation of a number of the most important parameters of gas exchange, and the indicators of gas exchange in general, determines the need for further research on a whole complex of interrelated problems of pathogenesis and therapy of respiratory diseases.

Objective: to study morphofunctional changes in liver tissue, in the dynamics of the use of ozonized water in rats in an experimental model of chronic purulent pneumonia.

## MATERIALS AND METHODS

Used 30 male outbred white rats weighing 180-200 g. Animals are divided into 3 groups. In the first group (n = 10) healthy rats were injected intraperitoneally with 5 ml of ozonated (0.02 mg / l) 0.9% sodium chloride solution once a day for 10 minutes. The course of treatment is 10 days. Animals of the second (n = 10) and third (n = 10) groups were first modeled with e-CIL. The e-CIL model was reproduced by the method of Z. Batyrova and N. Shamirzaeva [2]. For this, under sterile conditions, under local novocaine anesthesia, a longitudinal incision 1.5-2.0 cm long was made along the midline on the anterior surface of the animal's neck. After exposing the anterior wall of the trachea between its rings, a nylon thread with a diameter of 0.4 mm and a length of 10-12 cm was inserted into its lumen on a thin piercing needle. The distal end of the thread was in the lumen of the trachea, and its proximal end was fixed on the skin. The wound was sutured tightly in layers. After 45 days from the beginning of the experiment, the fixing thread was removed by cutting with forceps without opening the trachea.

Subsequently, the animals of the second group did not receive treatment.

The animals of the third group, 45 days after the reproduction of e-CIL, were injected once a day with ozonized (0.02 mg / l) 0.9% sodium chloride solution for 10 minutes into the peritoneum, 5 ml each. The course of treatment is 10 days.

For ozone therapy we used an ozonator - «Binafsha».

The animals were removed from the experiment by instant decapitation.

The taken pieces of the liver were fixed in formalin. Histological sections were stained with hematoxylin and eosin. Microscopy was performed using an XS-213 light microscope and a Leica microscope.

## RESULTS AND DISCUSSION

E-CIL manifested itself in the form of distant wheezing, disturbances in the frequency of breathing rhythm and inactivity of the subjects. Macropicture: lungs without atelectasis, in places of a pale gray-red or dark red color, a doughy consistency, under the pleura and in the parenchyma, small hemorrhages are often found. On the cut, a frothy, turbid liquid, sometimes colored pink, is squeezed out of the lumens of the cut bronchi and flows down. The surface of the lung is smooth, juicy, gray or dark red, against which the expanded gelatinous cords of the infiltrated interstitial connective tissue with serous exudate clearly stand out. The liver is not enlarged, the surface is smooth, dark cherry-colored in section (Fig. 1). Microscopically, 80% of large and 20% of small hepatocytes were found in the liver tissue.

In animals of the second group with e-CIL without treatment, in contrast to healthy animals of the first group, characteristic changes were observed in the liver, resembling a picture of acute toxic liver damage. Many hepatocytes were in a state of pronounced balloon dystrophy, with damage to the nuclei, which was expressed by karyopycnosis, and multiple foci of parenchymal necrosis were identified. Sinusoids were practically not visible due to an increase in the volume of dystrophically swollen hepatocytes. The chaotic arrangement of hepatocytes of the hepatic lobules was also characteristic. In addition, lack of blood circulation of the central veins and vessels of the triads was also determined (Fig. 2).

At the initial stages of treatment, the phenomena of balloon dystrophy of the liver persist (Fig. 3).

After a course of ozone therapy, regular changes are observed in the morphological picture of the liver tissue, expressed in a gradual improvement in the state of the tissue, which correlates with the duration of therapeutic measures. Thus, noticeable improvement in the state of the structure of the liver tissue in the group treated with ozone therapy attracted attention. These changes were characterized by a decrease in the manifestations of hydropic dystrophy and focal necrosis of hepatocytes, restoration of the normal trabecular-beam architectonics of the hepatic lobules (Fig. 4, 5).

By the 30th day after the completion of treatment, the state of the parenchymal elements and blood circulation in the liver significantly improved. Signs of balloon dystrophy decreased, although swelling of hepatocytes was still preserved, granular degeneration of cells appeared. Hepatic lobules acquire a characteristic beam structure. These changes indicate the activation of reparative recovery processes. Impaired blood circulation is also restored (Fig. 6). In places the sinusoids are

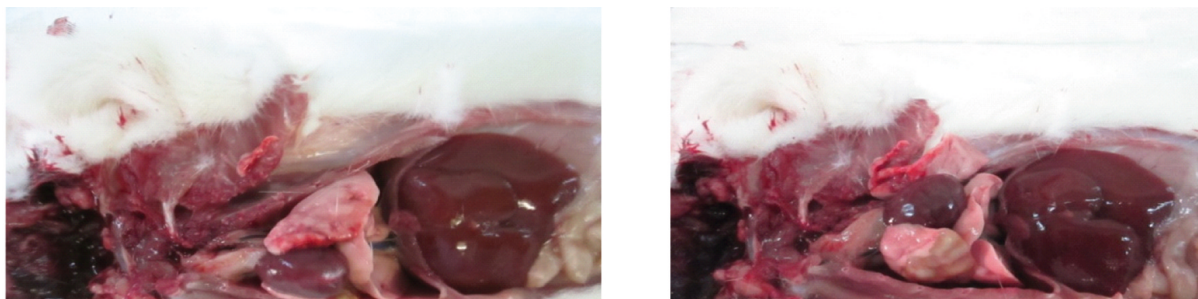


Fig.1. Purulent inflammation of the lobe of the lung on the 45th day of calling the E-CIL model.  
The liver is not enlarged, smooth.

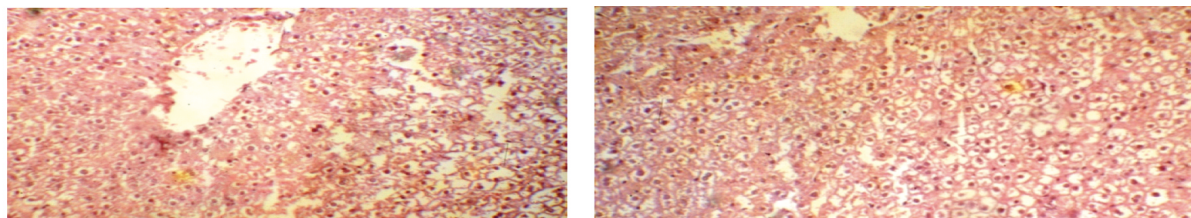


Fig. 2. Liver of rat with E-CIL before treatment. Balloon dystrophy and focal necrosis of hepatocytes.  
Liver tissue anemia. Coloring: hematoxylin-eosin.  
Zoom: 10x10.

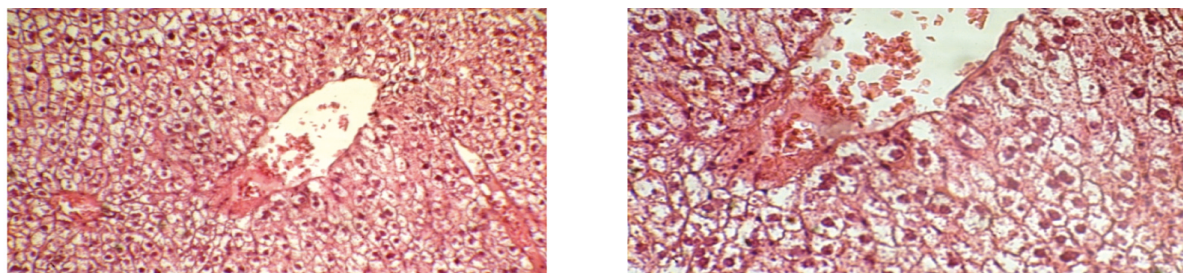


Fig. 3. Liver of E-CIL rats after treatment, initial terms.  
The phenomena of balloon dystrophy persist. Zoom: 10x10, 20x10.

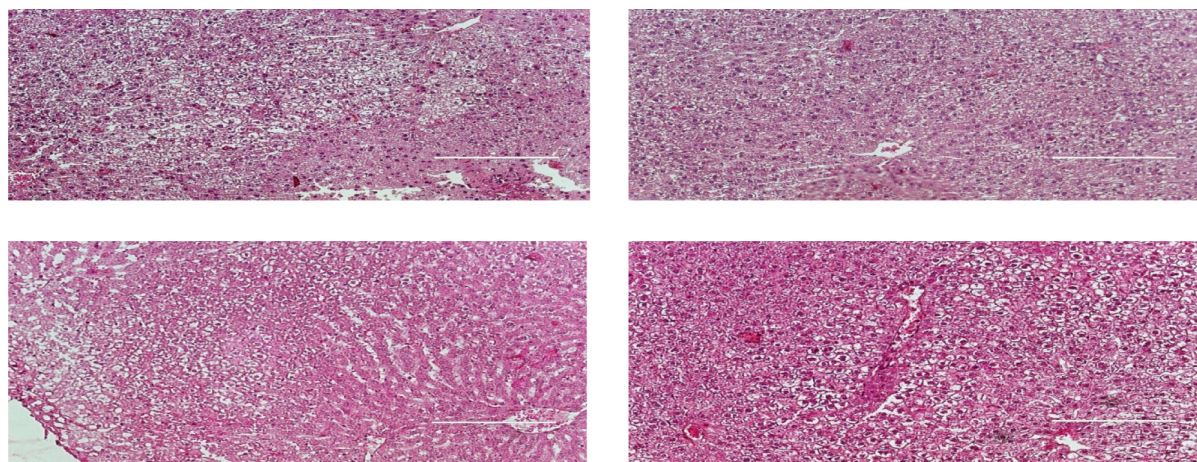


Fig. 4. Liver of rats with E-CIL model. Diffuse hydropic dystrophy and focal necrosis of hepatocytes.  
Violation of the beam structure of the lobules. Coloring: hematoxylin-eosin.  
Zoom: 10x20, 10x40.

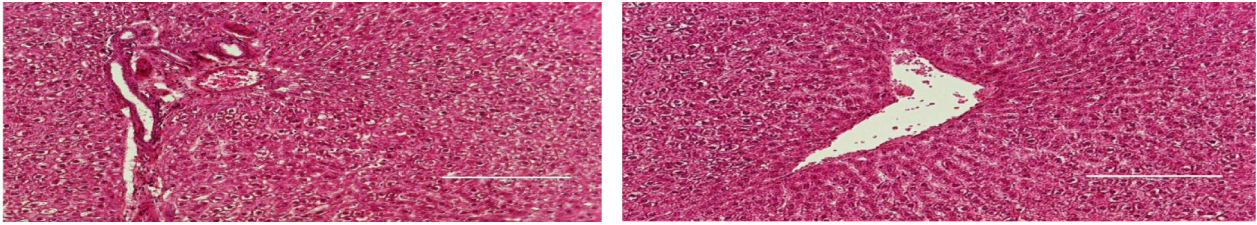


Fig. 5. Rat liver after a course of ozone therapy. Restoring normal cytoarchitectonics of liver tissue. Reduction of dystrophic manifestations. Coloring: hematoxylin-eosin. Zoom: 10x20.

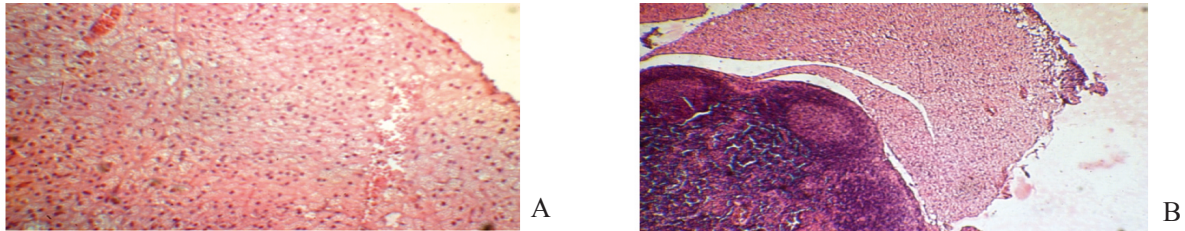


Fig. 6. Liver of E-CIL rats on the 30th day after completion of treatment. A. Swelling and granular dystrophy of hepatocytes, expansion of sinusoids with plethora; B – hyperplasia of the lymph node follicles of the hepatic hilum. Coloring: hematoxylin-eosin. Zoom: 10x20.

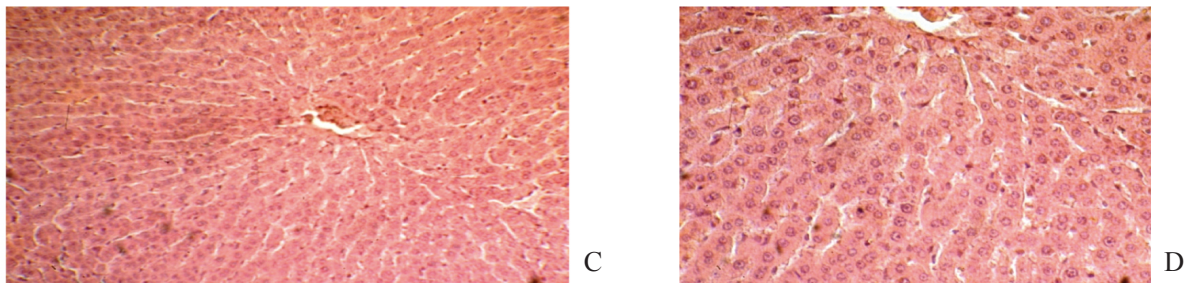


Fig.7. The liver of an E-CIL rat on the 30th day after completion of treatment. C, D – beam structure of hepatic lobules, vascular congestion. Zoom: 10x10, 20x10.

sharply expanded with plethora. The central veins are also full-blooded (Fig. 7). Hyperplasia of lymphoid structures is observed in the liver tissue by the 30th day after completion of treatment.

### CONCLUSIONS

1. In rats, experimental chronic inflammation of the lungs caused by prolonged mechanical irritation of the respiratory tract causes structural changes in the liver characteristic of toxic hepatitis.
2. A 10-day course of treatment with ozonized saline improves the morphological picture of the rat liver.
3. In healthy rats, a 10-day course of ozone therapy does not adversely affect the general condition and behavior of the animals.

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### REFERENCES

1. Abdrashitova E.Kh. [Morphological characteristics of spontaneous chronic respiratory disease in rats] // *Biomedicina*. 2006; 1 (2). [in Russian]. <http://cyberleninka.ru/article/n/morfologicheskaya-harakteristika-spontannoy-hronicheskoy-respiratornoy-bolezni-krysa>
2. Batyrova Z.B., Shamirzaev N.Kh. [A method for modeling chronic nonspecific pneumonia] // 2002. Patent v 20420502 a2. [in Russian].
3. Babaev Kh., Orazbaev Sh. [On the effectiveness of ozone therapy in the treatment of purulent wounds of soft tissues] // *Young scientist*. 2011 Sep; 9(32): 235-41. [in Russian]. <https://moluch.ru/archive/32/3635/>
4. Karimov M.M., Abdullaev A.Kh., Sabirova G.N. [et al] [The use of ozone therapy in the rehabilitation treatment of patients with chronic hepatitis] // *Method. recom*. Tashkent, 2007. 9 p. [in Russian].
5. Malenkov A.G. [Influence of ozone on the human body and the mechanisms of its therapeutic action] //

- Moscow, 2011. [in Russian]. <http://magericmed.net/vliyanie-ozona-na-organizm-cheloveka-i-mexanizmy-ego-lechebnogo-dejstviya.html>
6. Kulikov A.G. [Ozone therapy is an integral part of physiotherapy] // Physiotherapy, balneology, rehabilitation. 2005; 4: 3-7. [in Russian]. <https://elibrary.ru/item.asp?id=17112525>
  7. Peretyagin S.P., Kostina O.V., Martusevich A.A., Didenko N.V. Influence of inhalation with reactive oxygen species on pro- and antioxidant balance in the lungs of experimental animals // Medical Almanac. 2013; 3 (27): 65-7. [in Russian]. <https://cyberleninka.ru/article/n/vliyanie-ingalyatsiy-aktivnymi-formami-kisloroda-na-proi-antioksidantnyy-balans-v-legkih-eksperimentalnyh-zhivotnyh/viewer>
  8. Puzin S.N., Tangieva Kh.I., Zavolovskaya L.I. [Features of dynamics and structure of repeated disability due to respiratory diseases] // Mat. scientific. conf. «Equal Opportunities». M., 2009, 51-3. [in Russian].
  9. Strukov P.V., Kulikov A.G., Zubkova A.V. [Normobaric hypoxia, ozone therapy and breathing exercises with expiratory resistance in the rehabilitation treatment of patients with chronic bronchitis and bronchial asthma] // Questions of balneology, physiotherapy and physiotherapy exercises. 2004; 4: 7-11. [in Russian]. <http://www.fesmu.ru/elib/Article.aspx?id=113517>
  10. [Chernekhovskaya N.E., Shishlo V.K., Povalyaev A.V. Experimental and morphological studies of reparative regeneration of the tracheal epithelium, diffuse lymphoid tissue and regional lymph nodes under ozone therapy] // Bulletin of lymphology. 2006; 1: 34-8. [in Russian]. [https://lymphology-journal.com/catalog/detail.php?SECTION\\_ID=762&ID=16583](https://lymphology-journal.com/catalog/detail.php?SECTION_ID=762&ID=16583)
  11. Momot A.P., Shoikhet Ya.N. [On the role and relationship of hemostatic and inflammatory reactions in the formation of foci of purulent destruction of organs and tissues] // Problems of Clinical Medicine. 2008; 4: 102-18. [in Russian]. <http://www.fesmu.ru/elib/Article.aspx?id=191787>

## ОСОБЛИВОСТІ МОРФОЛОГІЧНИХ ПОКАЗНИКІВ ПЕЧІНКИ ПРИ ХРОНІЧНОМУ ГНІЙНОМУ ЗАПАЛЕННЯ ЛЕГЕНІВ У ДИНАМІЦІ ОЗОНОТЕРАПІЇ (ЕКСПЕРИМЕНТАЛЬНЕ ДОСЛІДЖЕННЯ)

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**Актуальність.** Озон підвищує кисневотранспортну функцію крові. Перспективним є застосування озонотерапії при легеневої патології. Ефект озонотерапії пов'язаний зі здатністю озону до ліквідації гіпоксемії і гіпоксії тканин, яка завжди є у хворих з патологією бронхо-легеневого апарату.

**Мета:** вивчити морфофункціональні зміни тканини печінки, в динаміці застосування озонованої води у щурів в експериментальній моделі хронічного гнійного запалення легенів.

**Матеріали та методи.** 3 30 самців білих щурів (180-200 г) сформували 3 групи. В 1 групі (n=10) здоровим щурам один раз на день внутрішньочеревино вводили по 5 мл озонованого (0,02 мг/л) 0,9 % NaCl протягом 10 хв. Курс 10 днів. Тваринам 2 (n=10) і 3 (n=10) груп спочатку моделювали хронічне запалення легенів. Для цього під місцевою новокаїновою анестезією на шії тварини робили розріз завдовжки 1,5-2,0 см. У просвіт трахеї, між її кільцями вводили на тонкій колючій голці капронову нитку діаметром 0,4 мм, довжиною 10-12 см. Дистальний кінець нитки знаходився в просвіті трахеї, а проксимальний її кінець закріплювали на шкірі. Рану поширено ушивали наглухо. Через 45 днів нитку витягували без розтину трахеї. Надалі тварини 2 групи лікування не отримували. А щурам 3 групи один раз на добу вводили 5 мл озонованого (0,02 мг/л) 0,9 % NaCl протягом 10 хв. Курс 10 днів. З експерименту тварин виводили шляхом миттєвої декапітації. Взяті шматочки печінки фіксували у формаліні. Гістологічні зрізи фарбували гематоксилін еозин. Мікроскопію проводили в світловому мікроскопі XS-213 і мікроскопі Leica.

**Результати.** При тривалому подразненні дихальних шляхів виявлено структурні зміни печінки, характерні для токсичного гепатиту. Після лікування озонованим фізіологічним розчином відбувалося поліпшення морфологічної картини печінки. У здорових щурів озонотерапія не чинила негативного впливу на загальний стан і поведінку тварин.

**Висновки.** Лікування озонованим фізіологічним розчином покращує морфологічну картину печінки щурів з хронічним запаленням легенів.

**Ключові слова:** хронічне запалення легенів, щури, озонотерапія, морфологія, печінка.

**ОСОБЕННОСТИ МОРФОЛОГИЧЕСКИХ ПОКАЗАТЕЛЕЙ ПЕЧЕНИ  
ПРИ ХРОНИЧЕСКОМ ГНОЙНОМ ВОСПАЛЕНИИ ЛЁГКИХ В ДИНАМИКЕ ОЗОНОТЕРАПИИ  
(ЭКСПЕРИМЕНТАЛЬНОЕ ИССЛЕДОВАНИЕ)**

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**Актуальность.** Озон повышает кислородтранспортную функцию крови. Перспективным является применение озонотерапии при легочной патологии. Эффект озонотерапии связан со способностью озона к ликвидации гипоксемии и гипоксии тканей, которая всегда имеется у больных с патологией бронхолегочного аппарата.

**Цель:** изучить морфофункциональные изменения ткани печени, в динамике применения озонированной воды у крыс в экспериментальной модели хронического гнойного воспаления лёгких.

**Материалы и методы.** Из 30 самцов белых крыс (180-200 г.) сформировали 3 группы. В 1 группе (n=10) здоровым крысам один раз в день внутривентриально вводили по 5 мл озонированного (0,02 мг/л) 0,9 % NaCl в течение 10 мин. Курс 10 дней. Животным 2 (n=10) и 3 (n=10) групп сначала моделировали хроническое воспаление лёгких. Для этого под местной новокаиновой анестезией, на шею животного делали разрез длиной 1,5-2,0 см. В просвет трахеи, между её кольцами вводили на тонкой колющей игле капроновую нить диаметром 0,4 мм, длиной 10-12 см. Дистальный конец нити находился в просвете трахеи, а проксимальный ее конец закрепляли на коже. Рану послойно ушивали наглухо. Через 45 дней нить извлекали без вскрытия трахеи. В дальнейшем животные 2 группы лечения не получали. А крысам 3 группы один раз в сутки вводили 5 мл озонированного (0,02 мг/л) 0,9 % NaCl в течение 10 мин. Курс 10 дней. Из эксперимента животных выводили путём мгновенной декапитации. Взятые кусочки печени фиксировали в формалине. Гистологические срезы окрашивали гематоксилин эозином. Микроскопию проводили в световом микроскопе XS-213 и микроскопе Leica.

**Результаты.** При длительном раздражении дыхательных путей выявлены структурные изменения печени, характерные для токсического гепатита. После лечения озонированным физиологическим раствором происходило улучшение морфологической картины печени. У здоровых крыс озонотерапия не оказывала отрицательного воздействия на общее состояние и поведение животных.

**Выводы.** Лечение озонированным физиологическим раствором улучшает морфологическую картину печени крыс с хроническим воспалением лёгких.

**Ключевые слова:** хроническое гнойное воспаление лёгких, крысы, озонотерапия, морфология, печень.

## CHANGES OF COGNITIVE FUNCTION IN PATIENTS WITH HYPERTENSION WITH CONCOMITANT DIABETES MELLITUS TYPE 2

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**Relevance.** Till now there is no clear clinical trial understanding of the relationship between hypertension (AH) and the patient's cognitive function.

**Objective:** investigation of changes in cognitive function in patients with hypertension with concomitant type 2 diabetes mellitus (DM2).

**Materials and methods.** 215 people were examined: Group I (n = 131) – stage II hypertensive disease (HD); Group II (n = 46) – HD, combined with diabetes mellitus2; Group III, control (n = 38) – without a diagnosis of HD and diabetes mellitus2. All examined blood pressure (BP), echocardiogram. Clinical complaints, anamnestic data, and neuropsychiatric testing data were used to diagnose moderate cognitive impairment (MCI). Used modified diagnostic criteria J. Touchon, R. Petersen. To assess cognitive function used: Short scale of assessment of mental state (Mini-Mental State Examination - MMSE); Frontal Assessment Battery (FAB); clock drawing test; test for literal and categorical associations; Schulte tables; the Global Deterioration Scale (GDS) and the Clinical Dementia Rating (CDR).

**Result.** In patients with HD, the most significant risk factors for moderate cognitive impairment are hypercholesterolemia and overweight (with OR 1.8), obesity (OR 1.6), the presence of concomitant diabetes mellitus2, which, especially in overweight, significantly impairs cognitive function (OR 2.56). Deterioration of cognitive function correlates with the duration of HD, cholesterol levels. Concomitant diabetes mellitus2 in patients with HD creates a statistically significant additional negative effect on the results of cognitive function. In patients with HD with a distorted daily blood pressure profile, the neurodynamic component of cognitive function is first of all affected - conceptualization, repetition, reaction of choice. The relationship between cognitive function and daily monitoring of blood pressure often have a U-shaped relationship, where the maximum indicators of cognitive function are at the level of the optimal recommended blood pressure figures (130-139 mm Hg for SBP, and 75-85 mm Hg for DBP, and the daily index within 10%).

**Conclusions.** There is a dependence of changes in cognitive function on the presence of risk factors and signs of subclinical damage to target organs. The nonlinear U-shaped character of the relationship between the average daily, average night and average daily blood pressure and the results of screening tests and scales for assessing cognitive function is shown.

**Key words:** arterial hypertension, cognitive functions, type 2 diabetes mellitus

**Relevance.** Hypertension (AH) is an urgent problem among the working age population and the most important risk factor for acute cerebrovascular disorders, as well as a harbinger of Alzheimer's disease, vascular dementia and other cognitive disorders [1]. The relationship between cognitive impairment, including dementia of various etiologies, and blood pressure (BP) and the need for adequate antihypertensive therapy to prevent them is being investigated. To date, there is no clinical trial based clear understanding of the relationship between blood pressure and cognitive function [2, 3, 4]. While most long-term studies have shown elevated blood pressure before occurrence of Alzheimer's disease or vascular dementia and other cognitive impairment, most crossover and short-term studies have shown an association between low blood pressure and dementia or no association with blood pressure. and cognitive impairment. There

are no data on the effect of antihypertensive therapy on cognitive function, and studies on this issue are few and contradictory [5].

Thus, the identification of general patterns of formation of cognitive disorders in patients with hypertension and assessment of the possibility of their correction on the background of antihypertensive therapy is an urgent interdisciplinary medical problem.

**Objective:** investigation of changes in cognitive function in patients with hypertension with concomitant type 2 diabetes mellitus (DM2).

### MATERIALS AND METHODS

A total of 215 people were examined. Of these – 177 patients with hypertension (HD) and 38 people without HD. Patients with HD were divided into 2 groups: Group I (n = 131) – HD stage II; Group II (n = 46) – HD,

combined with diabetes mellitus<sup>2</sup>. The duration of HD in groups I and II ranged from 6 months to 37 years. Group III (or control group) (n = 38) included patients with mild somatic pathology without a diagnosis of HD and diabetes mellitus<sup>2</sup> (according to the results of clinical, laboratory and instrumental examinations), comparable in age, sex, level of education with groups I and II.

The mean age of patients was  $50.4 \pm 11.7$  years.

According to the purpose of the study, patients were further divided into subgroups:

In group I (stage II HD), 20 patients (15.3%) had grade 1 HD, and 111 patients (84.7%) had grade 2 HD;

In group II (stage II HD + diabetes 2) 6 patients (13%) had 1 degree of HD, and 40 patients (87%) – 2 degree of HD;

Within 24 hours, all patients underwent blood pressure monitoring, echocardiographic examination of the heart, for the diagnosis of moderate cognitive impairment (MCI) used clinical complaints, anamnestic data and neuropsychiatric testing data. Syndromic diagnosis establishes the fact of reduced cognitive abilities in comparison with the individual norm with an assessment of the severity of cognitive impairment. The starting point in the syndromic diagnosis of cognitive impairment in most cases are complaints of memory loss or mental retardation [6].

When diagnosing «MCI syndrome» used modified diagnostic criteria J. Touchon, R. Petersen, 2004 [7, 8].

Commonly used for clinical trials and validated tests and scales were used to assess cognitive function, namely: The Mini-Mental State Examination (MMSE) proposed by M.F. Folstein, S.E. Folstein, P.R. Hugh, 1975; Frontal Assessment Battery (FAB), proposed by B. Dubois, 1999; clock drawing test; test for literal and categorical associations; Schulte tables; the Global Deterioration Scale (GDS) and the Clinical Dementia Rating (CDR).

## RESULTS AND DISCUSSION

Patients were interviewed for complaints of memory, attention, orientation, memory and thinking speed impairment. Patients were asked to self-assess these indicators of cognitive function on a five-point scale from 1 to 5 points, where 1 point – a significant deterioration, and 5 points – the absence of any complaints. According to the results of data processing, in the group of patients with HD without diabetes mellitus on all complaints is dominated by 4 points, followed by the frequency of presentation – 5 points and 3 points. At the same time, in the group of patients with HD with concomitant diabetes mellitus, the predominant indicator is 3 points, followed by the frequency of presentation – 4 and 2 points for the vast majority of indicators.

It was found that in patients with HD the most common complaints were of memory impairment (22.4% of patients rated the function on 3 points, 44.7% – 4 points), 27.6% of patients did not complain of memory impairment at all, thus, complaints of memory impairment, regardless of severity, were found in 72.4% of patients.

In second place were the difficulty of mentioning and orientation impairment (19.7% of respondents on both indicators rated the condition at 3 points), in third place in the frequency of presentation were complaints of decreased speed of thinking (17.1% – 3 points, 39.5% – 4 points), there were no complaints of impaired thinking (5 points) in 88% of patients (Fig. 1).

In the second group of patients – patients with HD and concomitant diabetes mellitus 2 – the frequency of complaints was as follows (Fig. 2).

The lowest score was obtained for the deterioration of the function of thinking speed, 20% of patients rated the function at 2 points, 42.8% – at 3 points, only 17.1% had no complaints (5 points). Complaints of memory impairment were rated 3.1% of patients, 42.8% of patients rated the speed of thinking at 3 points, and only 14.3% of patients did not complain of memory impairment. The least affected functions in patients of the second group were the difficulty of mentioning and impaired orientation – 42.8% on both indicators received 3 points.

In the control group, patients had no complaints of memory impairment, speed of thinking, orientation, attention and difficulty remembering, a small proportion of patients had a score of 4 points.

Among the examined patients in the first study group, the criteria of the syndrome of moderate cognitive impairment were found in 23 patients (17.56%), in the second group of patients with HD and concomitant diabetes mellitus – in 26 patients (56.52%), at the same time in the group control under these criteria fell 1 person, which is 2.63%. The obtained data are comparable with the literature sources of persons of the appropriate age category and the presence of relevant risk factors.

Thus, cognitive function in general in patients with HD is statistically significantly reduced compared with the control group, which is representative of the main parameters. Also, a comparison of groups I and II revealed statistically significantly worse results in group II for most screening tests and scales, except for the sample for literal and categorical associations.

Consider the influence of different risk factors on the cognitive function of patients with HD and in patients with HD and concomitant diabetes mellitus<sup>2</sup> (Table 1). Risk factors whose effect on cognitive function we studied include, according to the recommendations of the European Society of Cardiology: obesity (BMI  $\geq 30$  kg / m<sup>2</sup>), overweight (BMI  $\geq 25$  kg / m<sup>2</sup>), smoking, hypercholesterolemia (more than 4.9 mmol / l), left ventricular hypertrophy (LV) (for men IMMLV > 115 g / m<sup>2</sup>, for women IMMLV > 95 g / m<sup>2</sup>). To analyze the risk and chance of moderate cognitive impairment (MCI) in the presence of various risk factors, we use the method of bipolar tables.

Notes: SMCI – syndrome of moderate cognitive impairment, HD- hypertension, CD2 – type 2 diabetes, LV – left ventricle

Among all risk factors in the examined patients, LV hypertrophy was most common in both men and

women – 81% and 80%, respectively. In second place in terms of frequency among risk factors was overweight – 78%, hypercholesterolemia – 71%.

Smoking and obesity among patients in the study population were observed in 34% and 35%, respectively (Fig. 3).

In addition, type 2 diabetes, as a recognized risk factor, creates an additional negative impact on cognitive function in combination with HD. There is a cumulative effect, which leads to significantly worse indicators of cognitive function testing compared with patients with HD without diabetes, the results of which are also significantly

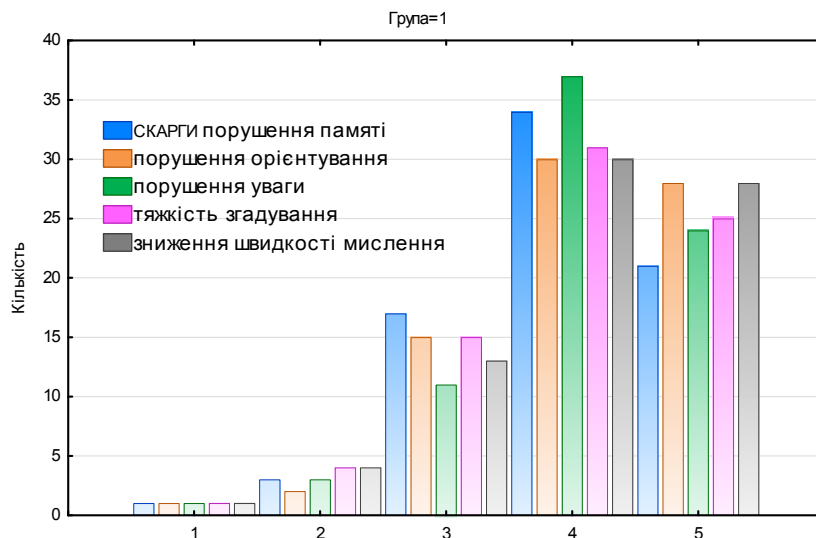


Fig. 1. Frequency of complaints of patients with cognitive impairment in group I (HD)

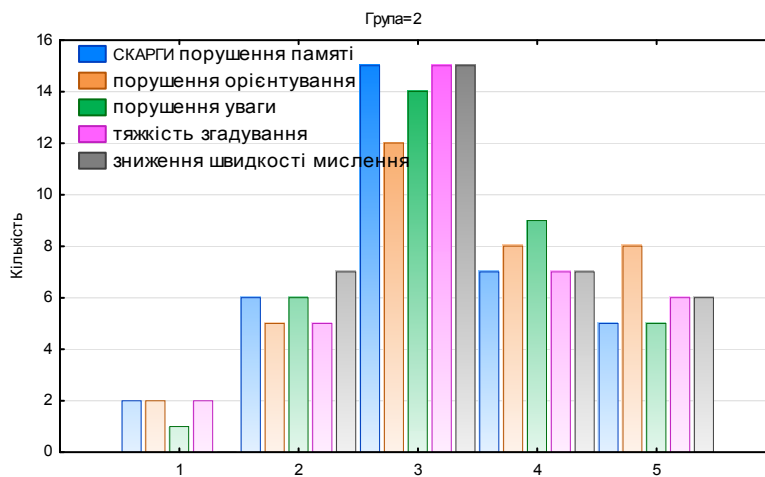


Fig. 2. Frequency of complaints of patients with cognitive impairment in group II (HD + CD2)

Table 1  
Distribution of risk factors for the development of moderate cognitive impairment in patients with hypertension

Risk factor and its presence		group 1 (HD), n=131		group 2 (HD+DM2), n=46	
		SMCI	No SMCI	SMCI	No SMCI
Smoking	yes	4	48	3	5
	no	19	60	23	15
Obesity & overweight (BMI ≥ 25kg / m2)	yes	16	84	23	15
	no	7	24	3	5
Obesity (BMI ≥ 30kg / m2)	yes	10	34	17	1
	no	13	74	9	19
Hypercholesterolemia	yes	21	76	9	10
	no	4	30	5	8
LV hypertrophy (male)	yes	18	55	6	14
	no	1	19	1	1
LV hypertrophy (female)	yes	7	15	4	2
	no	4	3	0	0

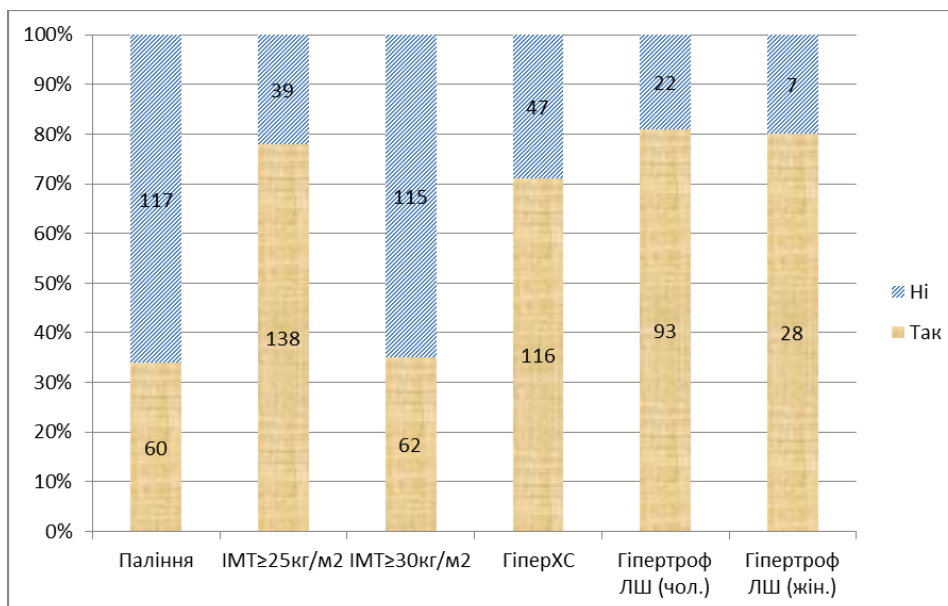


Fig. 3. Distribution of study patients depending on the presence of risk factors

lower when comparing the mean values (or mode and median) compared with the control group.

Among 131 patients of the first group, 50 people had a normal level of blood pressure at night at 10-20%, which is 38.3% of the total number of patients, 2 patients had a daily profile of the type of over-dipper with a daily index of more than 20% (1, 7%). 68 patients had an insufficient level of nocturnal blood pressure lowering – a daily profile of the non-dipper type (51.7% of the total). And 11 (8.3%) patients had a night picker profile – an increase in night blood pressure above the daytime, daily index less than 0. The distribution of patients by groups is shown in Figures 2-5. That is, the vast majority of patients have a daily profile with insufficient nocturnal decrease of blood pressure.

Statistically significant groups differ from each other in the MMSE test (Kruskal-Wallis test:  $H = 19.38415$ ,  $N = 91$ ,  $p = 0.0002$ ); when multiple comparison of MMSE test results among subgroups with different profiles of daily blood pressure was found that in the group night picker ( $p = 0.059$ ), non-dipper ( $p = 0.0007$ ) and normal dipper ( $p = 0.005$ ) the results are different from the control group (normotonic), herewith a statistically significant difference between the groups night picker, non-dipper and normal dipper is absent (Fig. 4).

The analysis of the polynomial scatter plot showed that in patients with HD the relationship between cognitive function and daily monitoring is not linear, and therefore is not detected in routine comparative statistical processing between groups.

Thus, a U-shaped relationship was found between the average daily SBP and the MMSE test result (Fig. 5).

Analyzing the diagram, we can conclude that the best range of blood pressure, in which the maximum values

are observed when testing cognitive function, are in the range of 130-140 mm Hg systolic blood pressure. The average daily SBP below 120 mm Hg is associated with a decrease in MMSE scores. A similar, but steeper, «tail» of the curve found at SBP above 140 mm Hg. – with the growth of the average daily, the effectiveness of MMSE decreases extremely rapidly.

A similar effect observed when analyzing the results of the MMSE scale and the average daily DBP. Optimal for satisfactory cognitive function is the average daily DBP at the level of 75-85 mm Hg, when the indicators of cognitive function are maximum in the studied category of patients (Fig. 6, fig. 7)

Probably, the basis of these disorders and phenomena is a violation of hemodynamics and trophism of the brain, especially at night, accompanied by a decrease in cerebral blood flow [9].

## CONCLUSIONS

1. In patients with HD, the most significant risk factors for moderate cognitive impairment are hypercholesterolemia and overweight (with OR 1.8), obesity (OR 1.6), the presence of concomitant type 2 diabetes, which, especially in conditions of overweight, significantly impairs cognitive function (OR 2,56).

2. Cognitive function in patients with HD is statistically significantly lower according to the results of neuropsychological tests and scales compared to the representative control group. Deterioration of cognitive function correlates with the duration of HD, cholesterol levels.

3. Concomitant type 2 diabetes mellitus in patients with HD creates a statistically significant additional negative effect on the results of cognitive function both in comparison with the comparable control group and in

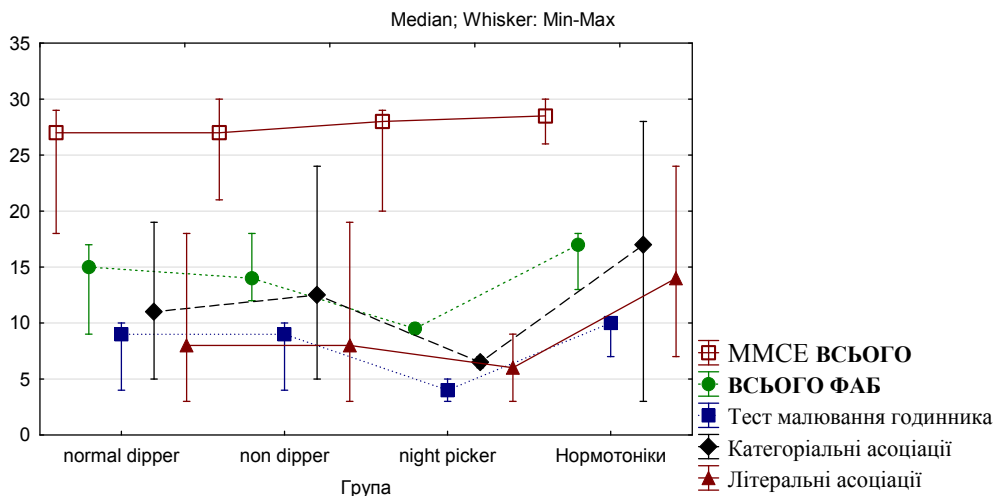


Fig. 4. Median and minimum-maximum values of tests and scales in groups of patients by type of daily profile

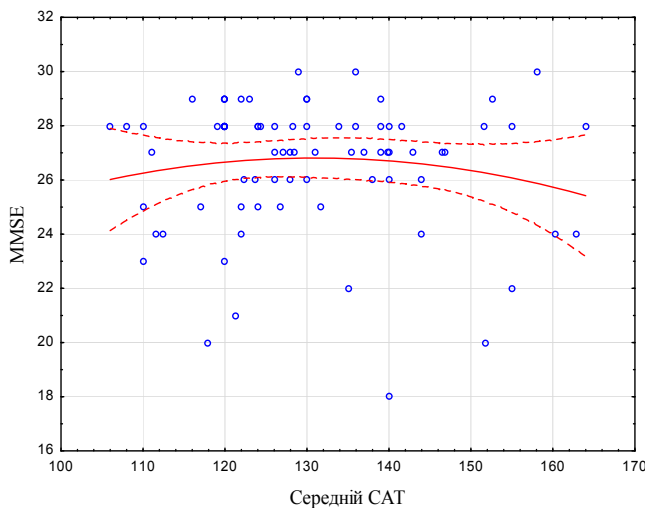


Fig. 5. Diagram of scattering of average daily CAT and scores based on the MMSE scale

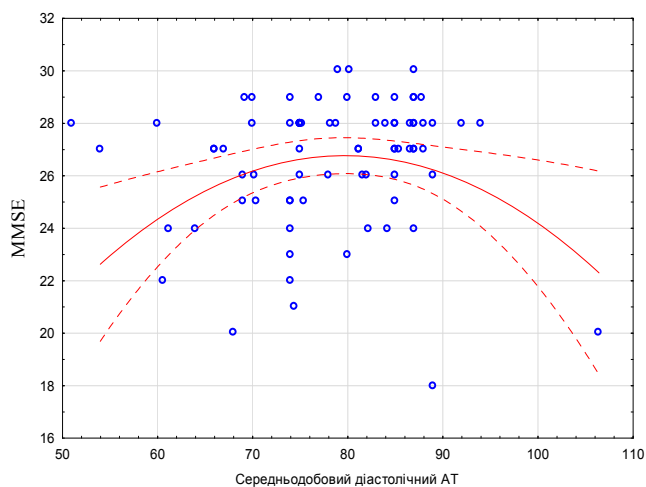


Fig. 6. Diagram of scattering of average daily DBP and scores according to the MMSE scale

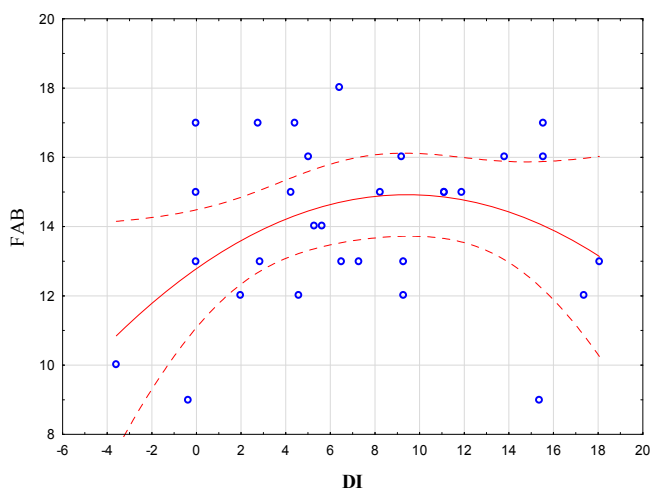


Fig. 7. Diagram of scattering of the daily index of blood pressure at night and scores on the FAB scale

comparison with the group of patients with HD without concomitant type 2 diabetes. Cognitive impairment in both subjects groups is mediated through neurodynamic subdomains and with signs of damage to the deep ganglia of the cerebral cortex.

4. In patients with HD with a distorted daily blood pressure profile, the neurodynamic component of cognitive function is first of all affected – conceptualization, repetition, reaction of choice. In addition, the relationship between cognitive function and daily monitoring of blood pressure often have a U-shaped relationship, where the maximum indicators of cognitive function are at the level of the optimal recommended blood pressure, which is 130-139 mm Hg for SBP, and 75- 85 mm Hg for DBP and daily index within 10%.

5. In patients with HD there is a U-shaped relationship between the mean values of average daily SBP and DBP, daily index and the results of screening tests and scales

for the diagnosis of cognitive impairment, with the maximum cognitive result in patients with HD observed at average SBP values in the range of 130-139 mm Hg and DBP 75-85 mm Hg at the level of night blood pressure decrease by 8-10%.

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## REFERENCES

1. Yakhno N.N., Zakharov V.V., Strachunskaya E.Ya., Velmeikin S.B., Zhitkova Yu.V., Ivanova I.L., Kurushina O.V., Pokhabov D.V., Svirkunova S.A. [Treatment of non-demented cognitive impairments in patients with arterial hypertension and cerebral atherosclerosis (According to the Russian multicenter study «FUETE»)] // Neurological Journal. 2012; 4: 49-55. [in Russian] <https://cyberleninka.ru/article/n/lechenie-nedementnyh-kognitivnyh-narusheniy-u-patsientov-s-arterialnoy-gipertenziy-i-tsebralnym-aterosklerozom-po-dannym>
2. Danaei G., Finucane M.M., Lin J.K., Singh G., Paciorek Ch.J., Cowan M.J., Farzadfar F., Stevens G.A., Lim S.S., Riley L.M., Ezzati M. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants // The Lancet. 2011 February 04; 377: 568-77. [https://doi.org/10.1016/S0140-6736\(10\)62036-3](https://doi.org/10.1016/S0140-6736(10)62036-3)
3. Nery A.B., Mesquita E.T., Lugon J.R., Kang H.Ch., de Miranda V.A., de Souza B.GT, Andrade J.AM, Rosa M.L.G. Prehypertension and cardiovascular risk factors in adults enrolled in a primary care programme // Eur. J. Cardiovasc. Prev. Rehabil. 2011 January 28; 18(2): 233-9. <https://journals.sagepub.com/doi/abs/10.1177/1741826710389380>
4. Landsberg L., Aronne L.J., Beilin L.J., Burke V., Igel L.I., Lloyd-Jones D., Sowers J. Obesity-related hypertension: Pathogenesis, cardiovascular risk, and treatment – A position paper of the The Obesity Society and the American Society of Hypertension // Obesity. 2013 Jan; 21 (1): 8-24. PMID: 23282121. <https://doi.org/10.1111/jch.12049>
5. Kivipelto M., Helkala E.L., Laakso M.P., Hänninen T., Hallikainen M., Alhainen K., Soininen H., Tuomilehto J., Nissinen A. Midlife vascular risk factors and Alzheimer's disease in later life: longitudinal, population based study / // BMJ. 2001 June 16; 322 (7300): 1447-51. PMID: 11408299. <https://doi.org/10.1136/bmj.322.7300.1447>
6. Virta J.J., Heikkilä K., Perola M., Koskenvuo M. Midlife cardiovascular risk factors and late cognitive impairment // European Journal of Epidemiology. 2013 March; 28(5): 405-16. DOI: 10.1007/s10654-013-9794-y
7. Moretti F., Ronchia D., Palmerb K., Forlani C., Morini V., Ferrari B., Dalmonte E., Atti A.R. Prevalence and characteristics of mild cognitive impairment in the general population. Data from an Italian population-based study: The Faenza Project // Aging & Mental Health. 2013 Oct.16; 17 (3): 267-75. <https://doi.org/10.1080/13607863.2012.732034>
8. The AGES-Reykjavik Study: The Prevalence of Amnesic MCI in an Elderly Population. – Haskoli Islands School of Health Sciences, 2009. 64 p.
9. Ostroumova O.D. Cognitive impairments in arterial hypertension and the possibilities of their correction // Doctor. 2011; 14: 33-8. [in Russian] <https://medi.ru/info/2388/>

## ЗМІНИ КОГНІТИВНОЇ ФУНКЦІЇ У ХВОРИХ НА ГІПЕРТЕНЗІЮ З СУПУТНІМ ЦУКРОВИМ ДІАБЕТОМ ТИПУ 2

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**Актуальність.** До сьогодні не існує чітко доведеного клінічними дослідженнями розуміння взаємозв'язку рівня артеріальної гіпертензії (АГ) та стану когнітивної функції пацієнта.

**Ціль:** дослідити зміни когнітивної функції у хворих на гіпертензію з супутнім цукровим діабетом типу 2 (ЦД2).

**Матеріали та методи.** Обстежено 215 осіб: I група (n=131) – гіпертензивна хвороба (ГХ) II стадії; II група (n=46) – ГХ, поєднана з ЦД2; III група, контролю (n=38) – без встановленого діагнозу ГХ та ЦД2. Усім досліджували артеріальний тиск (АТ), ехокардіограму. Для діагностики синдрому помірних когнітивних порушень (ПКП) використовували клінічні скарги, анамнестичні дані та дані нейропсихічного тестування. Користувалися модифікованими діагностичними критеріями J. Touchon, R. Petersen. Для оцінки когнітивної функції використані: Коротка шкала оцінки психічного стану (Mini-Mental State Examination – MMSE); Батарея лобної дисфункції (Frontal Assessment Battery – FAB); тест малювання годинника; тест на літеральні та категоріальні асоціації; таблиці Шульте; шкала глобального погіршення (Global Deterioration Scale – GDS) і клінічна рейтингова шкала деменції (Clinical Dementia Rating – CDR).

**Результат.** У хворих на ГХ найбільш значущими факторами ризику помірних когнітивних порушень встановлено гіперхолестеринемію та надмірну масу тіла (з OR 1,8), ожиріння (OR 1,6), наявність супутнього ЦД2, який особливо за умов надмірної маси тіла, значно погіршує когнітивні функції (OR 2,56). Погіршення результатів когнітивних функцій корелює з тривалістю ГХ, рівнем холестерину. Супутній ЦД2 у пацієнтів із ГХ створює статистично значимий додатковий негативний вплив на результати когнітивної функції. У пацієнтів із ГХ зі спотвореним добовим профілем АТ в першу чергу вражається нейроди-

намічна складова когнітивної функції – концептуалізація, повторення, реакція вибору. Взаємозв'язок когнітивної функції та показників добового моніторингу АТ найчастіше мають U-подібну залежність, де максимальні показники когнітивної функції знаходяться на рівні оптимальних рекомендованих цифр артеріального тиску (130-139 мм.рт.ст для САТ, та 75-85 мм.рт.ст. для ДАТ, та добовий індекс в межах 10%).

**Висновки.** Існує залежність змін когнітивної функції від наявності факторів ризику та ознак субклінічного ураження органів-мішеней. Показаний нелінійний U-подібний характер залежності між середньодобовим, середньонічним та середньоденним АТ та результатами скринінгових тестів та шкал для оцінки когнітивної функції.

**Ключові слова:** артеріальна гіпертензія, когнітивні функції, цукровий діабет 2 типу

## ИЗМЕНЕНИЯ КОГНИТИВНОЙ ФУНКЦИИ У БОЛЬНЫХ С ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ С СОПУТСТВУЮЩИМ САХАРНЫМ ДИАБЕТОМ 2 ТИПА

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**Актуальность.** До сих пор не существует четко доказанного клиническими исследованиями понимания взаимосвязи уровня артериальной гипертензии (АГ) и состояния когнитивной функции пациента.

**Цель:** исследовать изменения когнитивной функции у больных с гипертонической болезнью с сопутствующим сахарным диабетом 2 типа (СД2).

**Материалы и методы.** Обследовано 215 человек: I группа (n=131) – гипертоническая болезнь (ГБ) II стадии; II группа (n=46) – ГБ, с сопутствующим СД2; III группа, контроль (n = 38) – без установленного диагноза ГБ и СД2. Всем исследовали артериальное давление (АД), эхокардиограмму. Для диагностики синдрома умеренных когнитивных нарушений (УКН) использовали клинические жалобы, анамнестические данные и данные нейропсихического тестирования. Пользовались модифицированными диагностическими критериями J. Touchon, R. Petersen. Для оценки когнитивной функции использованы: Краткая шкала оценки психического состояния (Mini-Mental State Examination – MMSE); Батарея лобной дисфункции (Frontal Assessment Battery – FAB); тест рисования часов; тест на литеральные и категориальные ассоциации; таблицы Шульце; шкала глобального ухудшения (Global Deterioration Scale – GDS) и клиническая рейтинговая шкала деменции (Clinical Dementia Rating - CDR).

**Результат.** У больных ГБ наиболее значимыми факторами риска умеренных когнитивных нарушений установлено гиперхолестеринемия и избыточную массу тела (с OR 1,8), ожирение (OR 1,6), наличие сопутствующего СД2, который, особенно в условиях избыточной массы тела, значительно ухудшает когнитивные функции (OR 2,56). Ухудшение результатов когнитивных функций коррелирует с продолжительностью ГБ, уровнем холестерина. Сопутствующий СД2 у пациентов с ГБ создает статистически значимое дополнительное негативное влияние на результаты когнитивной функции. У пациентов с ГБ с искаженным суточным профилем АД в первую очередь поражается нейродинамическая составляющая когнитивной функции – концептуализация, повторение, реакция выбора. Взаимосвязь когнитивной функции и показателей суточного мониторинга АД чаще всего имеют U-образную зависимость, где максимальные показатели когнитивной функции находятся на уровне оптимальных рекомендованных цифр артериального давления (130-139 мм.рт.ст САД и 75-85 мм.рт. ст. для ДАД, и суточный индекс в пределах 10%).

**Выводы.** Существует зависимость изменений когнитивной функции от наличия факторов риска и признаков субклинического поражения органов-мишеней. Показан нелінійний U-образний характер залежності між середнесуточним, середньонічним і середньоденним АД і результатами скринінгових тестів і шкал для оцінки когнітивної функції.

**Ключевые слова:** артериальная гипертензия, когнитивные функции, сахарный диабет 2 типа.

## CHANGES OF LIFE QUALITY SCORE DEPENDING ON THE ARTERIAL HYPERTENSION DEGREE IN THE GENDER ASPECT

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**Relevance.** Hypertension is one of the most common chronic diseases, for which currently the goal of therapy is not so much recovery as improving circulatory function with a satisfactory quality of life.

**Objective:** to determine the impact of different degrees of hypertension on quality of life in female and male patients.

**Materials and methods.** 126 patients with arterial hypertension underwent examination, including 86 women (68%), 40 men (32%) aged 40 to 81 years (mean age  $61.9 \pm 0.3$  years). Arterial hypertension of I degree had 19 people (15.1%), II degree - 65 patients (51.6%), III degree - 42 people (33.3%). The control group consisted of 43 healthy individuals who did not differ from the main group in terms of demographics. Surveys of patients to assess quality of life conducted with the questionnaire SF-36 (Short Form-36) at each follow-up. Quality of life indicators have value in points.

**Results.** The analysis of quality of life indicators in the group of healthy people found that the level of quality of life in men is much higher than in healthy women: «physical pain», «role functioning» -  $P1-P2 > 0.5$ ; «Physical functioning» -  $P1-P2 < 0.001$ ; «Physical health» -  $P1-P2 > 0.5$ , except for the scale «general health» -  $P1-P2 < 0.05$  ( $77.2 \pm 3.02$  vs.  $63.75 \pm 2.81$ ).

The comparison of the quality of life of patients with hypertension of I degree and patients with arterial hypertension of III degree found reliable differences on the scales «Vitality» ( $P1-P3 < 0.001$ ), and «Social functioning» ( $P1-P3 < 0.5$ ). In patients with II and III degrees of arterial hypertension indicators of quality of life were low in themselves and differed on a scale «role functioning» of the questionnaire: «Vital force» ( $P2-P3 > 0.5$ ); «Role functioning» ( $P2-P3 < 0.5$ ); «Mental health» ( $P2-P3 > 0.5$ ).

Patients with hypertension of the I degree in comparison with arterial hypertension of the II degree had reliably higher indicators of quality of life on scales «vital force» ( $80.0 \pm 3.93$  points) and «role functioning» ( $77.1 \pm 4.04$  points), but reduced indicators of «social functioning» and «mental health» ( $48.7 \pm 7.35$  and  $47.41 \pm 2.39$  points, respectively).

Patients with hypertension of I degree and III degree showed reliable differences on the scales «vital force» ( $P1-P3 < 0.001$ ) and «social functioning» ( $P1-P3 < 0.5$ ); and patients with hypertension of II and III degrees showed significant decrease in all indicators of quality of life, especially on the scales «social functioning» and «mental health» (up to  $31.5 \pm 5.19$  and up to  $40.31 \pm 2.23$  points, respectively).

Patients with hypertension of I degree had decrease in general health ( $87.1 \pm 3.16$ ), physical function ( $82.6 \pm 2.86$ ), and physical pain ( $87.1 \pm 3.16$ ). Patients with II degree of hypertension had a significant reduction in role functioning ( $32.4 \pm 5.19$ ), physical pain, and general health ( $36.0 \pm 6.12$  and  $42.26 \pm 2.68$  points, respectively).

**Conclusions.** Hypertension significantly affects the quality of life. State of health of patients with hypertension significantly limited their physical activity.

**Key words:** arterial hypertension, quality of life, gender aspect, SF-36 questionnaire.

**Relevance.** Hypertension (AH) is one of the most significant health problems in the world, associated with complications such as stroke, myocardial infarction, heart and kidney failure, which cause high disability and significant economic costs [19, 25].

According to research, more than 30% of the adult population of Ukraine have high blood pressure (BP) [1, 2]. Regarding the official statistics of the Ministry of Health of Ukraine, as of January 1, 2016, 12,122,512 patients with hypertension registered in the country [3]. The prevalence of hypertension increases with age in both women and men [9]. Current guidelines recommend the same approaches to the treatment of hypertension, regardless of the patient's sex [5, 21, 22]. However, some studies show the existence of differences between men and women in the control of blood pressure and emphasize the need to form a different approach to the

management of patients with hypertension in females and males [8, 15-18, 20, 25]. In some cases, it is claimed that women have worse blood pressure control, in others, on the contrary, better [4, 6].

Studies on this problem suggest that postmenopausal women have a significant increase in blood pressure due to a sharp deterioration in the elastic properties of the arteries [7, 8, 10]. Increased vascular stiffness causes difficulties with blood pressure control [12, 23, 24].

Therefore, perhaps the reason for different blood pressure control may be the behavior and lifestyle of the patient, his ability to take advice and learn educational programs for the treatment of hypertension, different social status [11, 13, 14].

**Objective** of the study was to determine the effect of different degrees of hypertension on quality of life (QOL) in female and male patients with hypertension.

## MATERIALS AND METHODS

126 patients with hypertension underwent examination, including 86 women (68%), 40 men (32%) aged 40 to 81 years. The mean age of the subjects was  $61.9 \pm 0.3$  years. Patients divided into groups, depending on the degree of hypertension. Degree I hypertension (1 group) had 19 patients (15.1%), degree II hypertension (group 2) - 65 patients (51.6%), degree III hypertension (group 3) - 42 people (33.3%).

The control group consisted of 43 healthy individuals who did not differ from the main group in terms of demographics.

Patients included in the study examined 4 times. The duration of patient participation in the study was 14 weeks and included a selection visit followed by a 12-week treatment period.

The anamnesis collection was according to patient testimonies and medical records. Office blood pressure was measured in a sitting position in the morning, between eight and ten o'clock. Registration of systolic (SBP) and diastolic (DBP) BP was performed on the same arm three times with an interval of two minutes, if the BP values did not differ by more than 5 mm Hg. When detecting a larger difference between the obtained values, a fourth measurement was performed and the average value of three consecutive measurements was calculated. Heart rate (HR) was determined after the second measurement. Electrocardiogram (ECG) recording performed at the beginning of treatment and at the end.

At each visit, side effects recorded, the need to change antihypertensive therapy was determined.

Surveys of patients on quality of life assessment were conducted using the Medical Outcomes Study Short Form 36 questionnaire (SF-36, Russian version, with adapted Ukrainian translation, recommended by the International Center for Quality of Life Research) at each visit by patients themselves.

The questionnaire included 36 items, which were grouped into 8 scales: physical functioning (PF), role functioning (RF), physical pain (PP), general health (GH), vital force (VF), social functioning (SF), emotional state and mental health (MH). The patient chose the answer to the proposed question. Each answer had value in points. When forming one or another scale, these points added and mathematically processed by standard formulas. The scores on each scale range from 0 to 100, where 100 means complete health. The patient could choose several answers at once.

## RESULTS AND DISCUSSION

The main clinical and demographic characteristics of the patients included in the study presented in table 1.

As shows Table 1, the majority of patients included in the study were women with a mean age of  $63.1 \pm 0.6$ . The duration of hypertension in women and men did not differ significantly: it was in female  $9.4 \pm 0.4$ , in male  $8.6 \pm 0.4$ . Many patients with hypertension had comorbidities at the time of examination or in the anamnesis.

Table 1

The main clinical and demographic characteristics of the patients included in the study

Indicator, units of measurement	The indicator's value (M ± m)		P
	Male	Female	
Age, years	60,1 ± 0,3	63,1 ± 0,6	<0,01
Number of patients, n (%)	40 (31,7)	86 (68,3)	<0,005
The average level of SBP, mm Hg	158,80 ± 0,46	162,78 ± 0,32	>0,05
The average level of DBP, mm Hg	81,2 ± 0,3	82,60 ± 0,32	>0,05
Average heart rate, min-1	68,3 ± 0,3	74,2 ± 0,3	<0,05
Duration of hypertension, years	8,6 ± 0,4	9,4 ± 0,4	>0,05
Concomitant diseases, n (%)	42 (33,3)	84 (66,7)	<0,01
Regular alcohol consumption, n (%)	3 (7,5)	–	<0,0001
Salt abuse, n (%)	24 (60,0)	42 (48,8)	<0,0001
Regular physical activity, n (%)	6 (15,0)	8 (9,3)	<0,0001
Taking medication for hypertension, n (%)	22 (55,0)	54 (62,8)	<0,001
– of them regularly, n (%)	12 (54,5)	38 (70,4)	<0,05
Clinical signs of heart failure, n (%)	6 (15,0)	15 (17,4)	<0,0001
The presence of dyslipidemia, n (%)	34 (85,0)	78 (90,7)	<0,0001
Smoking:	15 (38,0)	11 (12,8)	>0,05
– duration of smoking, years	14,1 ± 0,26	12,4 ± 0,29	<0,01
– number of cigarettes, pcs/day	9,8 ± 0,19	6,2 ± 0,6	<0,01
Presence of close relatives with cardiovascular diseases at a young age, n (%)	8 (20,0)	14 (16,2)	<0,0005
Degree of AH, n (%)*:			
– I	7 (28,0)	10 (20,0)	<0,005
– II	10 (40,0)	23 (46,0)	<0,005
– III	8 (32,0)	17 (34,0)	<0,005

Note: \* - without taking into account the elderly

The level of SBP was significantly higher in female patients:  $162.78 \pm 0.32$ , compared with men, their SBP was  $158.80 \pm 0.46$  mm Hg. At the beginning of the study, the level of DBP and heart rate groups did not differ significantly. Note, that before inclusion in the study, only 12 men out of 22 (or 54.5%) and 38 women out of 54 (or 70.4%) regularly took antihypertensive drugs. This indicates that few people are aware of their hypertension, and even fewer are people who take antihypertensive treatment regularly.

In the general analysis of the surveyed groups it was found that among men with hypertension, compared with women, the frequency of smoking was higher - 1.75 times ( $P < 0.05$ ). The frequency of physical activity in men was 15% ( $P < 0.05$ ) against 9.3% ( $P > 0.05$ ) in women. Burdened heredity in the presence of cardiovascular disease in men was 8 (20%) against 14 in women (16.2%) ( $P < 0.0005$ ). Men were more likely to abuse salt - 60% vs. 48.8% ( $P < 0.0001$ ). Dyslipidemia was reported more often in women than in men - 90.7% vs. 85% ( $P < 0.0001$ ).

The results of the assessment of quality of life in patients using the SF-36 questionnaire shown in table 2.

Analysis of QOL in patients with hypertension (Table 2) found that patients with hypertension of I degree in comparison with hypertension of II degree had reliably ( $P < 0,001$ ) higher values of QOL on such scales as «vital force»:  $80.0 \pm 3.93$  points, and «role functioning»:  $77.1 \pm 4.04$  points. There are also slightly lower indicators

of social functioning and mental health -  $48.7 \pm 7.35$  and  $47.41 \pm 2.39$  points, respectively. In patients with hypertension of II and III degrees there is a significant decrease in all indicators of QOL, but especially - on the scales of SF and PH: up to  $31.5 \pm 5.19$  and up to  $40.31 \pm 2.23$  points, respectively. This indicates a significant impact of the disease on the patient's QOL.

When comparing the indicators of QOL in patients with hypertension of I degree and patients with hypertension of III degree, significant differences were found on the scales «vital force» (VF) ( $P_{1-P3} < 0,001$ ) and «social functioning» (SF) ( $P_{1-P3} < 0,5$ ). At patients of the II and III degrees of hypertension indicators of QOL were low in themselves and differed on the scale of RF of the questionnaire: VF ( $P_{2-P3} > 0,5$ ); SF ( $P_{2-P3} > 0,5$ ); RF ( $P_{2-P3} < 0,5$ ); PH ( $P_{2-P3} > 0,5$ ).

Thus, an increase in blood pressure above the first degree is associated with a decrease in QOL parameters in almost all components of the life of patients, which further indicates the need for appropriate correction of blood pressure.

Among the indicators that characterize the physical condition (Table 3), patients with hypertension of the I degree, first of all, increased the perception of GH ( $87.1 \pm 3.16$  points), PF ( $82.6 \pm 2.86$  points) and PP ( $87.1 \pm 3.16$  points).

At the same time, in the group of patients with hypertension of II degree there was a significant

Table 2

**Quality of life indicators for the component «psychological health» in patients with varying degrees of hypertension (according to the questionnaire SF-36)**

AH degree	Quality of life indicators, points, M ± m			
	VF	SF	RF	PH
Control group, n=43	97,6±0,92	96,7±2,68	84,6±1,26	98,8±2,46
I, n=19	80,0±3,93	48,7±7,35	77,1±4,04	47,41±2,39
II, n=65	56,6±3,54	31,5±5,19	56,0±3,29	40,31±2,23
III, n=42	53,9±4,7	34,5±6,08	57,56±3,86	36,9±2,79
Reliability of differences (P) between groups 1, 2, 3				
P <sub>1-P2</sub>	<0,001	>0,1	<0,1	<0,05
P <sub>1-P3</sub>	<0,001	>0,5	<0,05	<0,01
P <sub>2-P3</sub>	>0,5	>0,5	<0,5	>0,5
P <sub>k</sub>	>0,5	>0,5	<0,1	<0,5

Table 3

**Quality of life indicators for the «physical health» component in patients with varying degrees of hypertension (according to the SF-36 questionnaire)**

AH degree	Quality of life indicators, points, M ± m			
	PF	RF	PP	GH
Control group, n=43	96,4±0,86	94,6±2,18	92,6±1,42	98,8±0,54
I, n=19	82,6±2,86	68,7±4,02	87,1±3,16	88,2±2,78
II, n=65	54,2±4,68	32,4±5,19	36,0±6,12	42,26±2,68
III, n=42	49,8±3,4	28,6±4,12	47,1±3,92	28,8±4,16
Reliability of differences (P) between groups 1, 2, 3				
P <sub>1-P2</sub>	<0,001	>0,5	<0,1	<0,05
P <sub>1-P3</sub>	>0,5	<0,5	<0,05	<0,01
P <sub>2-P3</sub>	>0,5	>0,5	<0,5	>0,5
P <sub>k</sub>	>0,5	>0,5	<0,1	<0,5

**Quality of life indicators for the component «physical health» of patients with hypertension depending on gender (according to the questionnaire SF-36)**

Gender	Quality of life indicators, points, M ± m				
	PF	RF	PP	GH	PH
Healthy men, n = 9	97,78±0,88	97,22±2,78	94,17±3,91	77,2±3,02	52,78±6,51
Healthy women, n = 24	91,88±1,37	86,11±4,31	79,9±4,27	63,75±2,81	55,21±3,36
Sick men, n = 40	72,63±5,12	41,5±9,19	63,13±4,87	41,37±4,24	36,25±3,94
Sick women, n = 86	55,64±2,03	34,19±4,15	56,83±2,68	40,55±1,89	42,15±2,82
Reliability of differences (P) between groups					
P <sub>1</sub> -P <sub>2</sub>	<0,001	<0,05	<0,05	<0,01	>0,5
P <sub>3</sub> -P <sub>4</sub>	<0,001	<0,5	>0,5	>0,5	<0,5

decrease in such indicators as RF, PP and GH (32.4 ± 5.19; 36.0 ± 6.12 and 42.26 ± 2.68 points, respectively), which indicates that the physical activity of patients is significantly limited by the state of their health.

The analysis of QOL indicators in the group of healthy people found (Table 4) that the level of QOL in men is much higher than in healthy women: TB, RF (P<sub>1</sub>-P<sub>2</sub> > 0.5); PF (P<sub>1</sub>-P<sub>2</sub> < 0.001); physical health (PH) (P<sub>1</sub>-P<sub>2</sub> > 0.5), except for the scale GH, where P<sub>1</sub>-P<sub>2</sub> < 0.05, which indicates that the assessment of their health in healthy women is significantly lower than with men (77.2 ± 3.02 vs. 63.75 ± 2.81 points).

However, the QOL of men with hypertension is not significantly different from the QOL of women with hypertension, except for the PF index, which in men was 24% higher than in women (72.63 ± 5.12 vs. 55.64 ± 2.03 points). This may be due to the better physical development of men in general. Such dynamics of differences in the QOL rates of patients with hypertension of different sexes, compared with the control group, may indicate a greater degree of maladaptation of men in everyday life and a more pronounced weakening of their social contacts due to the disease.

The decrease in RF, which is due to physical condition, in men with hypertension to 63.13 ± 4.87, and in women to 56.83 ± 2.68 indicates that the daily activities of patients with hypertension of both sexes are significantly limited. There were no statistically significant differences in the study of PP indicators by gender and social status (P<sub>1</sub>-P<sub>2</sub> < 0.05 and P<sub>3</sub>-P<sub>4</sub> < 0.5, respectively).

## CONCLUSIONS

1. The level of quality of life in men in general is much higher (P < 0.05) than in women, except for the scale of general health.

2. In the component of psychological health in patients with hypertension I degree, compared with hypertension II degree, significantly higher indicators on the scale of vital force (80.0 ± 3.93 points) and role functioning (77.1 ± 4.04 points), but reduced indicators of social functioning and mental health (48.7 ± 7.35 and 47.41 ± 2.39 points, respectively).

3. In patients with hypertension I and III degrees, significant differences were found on the scales of vital force (P<sub>1</sub>-P<sub>3</sub> < 0.001) and social functioning (P<sub>1</sub>-P<sub>3</sub> < 0.5).

4. In patients with hypertension of II and III degrees there is a significant decrease in all indicators of quality of life, especially on the scales of social functioning and mental health (up to 31.5 ± 5.19 and up to 40.31 ± 2.23 points, respectively). This indicates a significant impact of hypertension on quality of life.

5. Patients with grade I hypertension had decreased general health (87.1 ± 3.16), physical function (82.6 ± 2.86), and physical pain (87.1 ± 3.16). Patients with grade II hypertension had a significant reduction in role functioning (32.4 ± 5.19), physical pain, and general health (36.0 ± 6.12 and 42.26 ± 2.68 points, respectively). This indicates a significant limitation of physical activity.

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## REFERENCES

- Mancia G., Fagard R., Narkiewicz K., et al. ESH/ESC Guidelines for the management of arterial hypertension // *Eur. Heart Jour.* 2013 July; 34 (Issue 28): 2159-219. <https://doi.org/10.1093/eurheartj/eh151>
- Hadley S., Petry J.J. Valerian // *Am. Fam. Physician.* 2003; 67(8): 1755-8. <https://www.aafp.org/afp/2003/0415/p1755.html>
- Asadujjaman M., Mishuk A.U., Hossain M.A., Karmakar UK. Medicinal potential of *Passiflora foetida* L. plant extracts: biological and pharmacological activities // *J. Integr. Med.* 2014 01 Mar; 12(2): 121-6. PMID: 24666678. DOI: 10.1016/s2095-4964(14)60017-0
- Noguchi Shinohara M., Ono K., Hamaguchi T., Iwasa K., Nagai T., Kobayashi Sh., Nakamura H., Yamada M. Pharmacokinetics, Safety and Tolerability of *Melissa officinalis* Extract which Contained Rosmarinic Acid in Healthy Individuals: A Randomized Controlled Trial // *PLoS One.* 2015 May 15; 10 (5): e0126422. PMID: 25978046. PMCID: PMC4433273. DOI: 10.1371/journal.pone.0126422

5. Bernatoniene J., Kopustinskiene D.M., Jakstas V., Majiene D., Baniene R., Kuršvietiene L., Masteikova R., Savickas A., Toleikis A., Trumbeckaite S. The effect of Leonurus cardiaca herb extract and some of its flavonoids on mitochondrial oxidative phosphorylation in the heart // *Planta Med.* 2014 May; 80 (7): 525-32. PMID: 24841965. DOI: 10.1055/s-0034-1368426
6. Treat-Jacobson D., Lindquist R.A., Witt D.R., Kirk L.N., Schorr E.N., Bronas U.G., Davey C.S., Regensteiner J.G. The PADQOL: development and validation of a PAD-specific quality of life questionnaire // *Vasc. Med.* 2012 Dec; 17(6): 405-15. PMID: 23184901. DOI: 10.1177/1358863X12466708
7. Dalfó Baqué A., Badia Llach X., Roca-Cusachs Coll A., Ruiz I Aristegui, Gamisans M Roset. [Validation of the quality of life questionnaire in arterial hypertension (HQALY) for its use in Spain. Relationship between clinical variables and quality of life. Investigator Group of the HQALY study] // *Aten. Primaria.* 2000 Jun 30; 26(2): 96-103. [Article in Spanish]. PMID: 10927826. DOI: 10.1016/s0212-6567(00)78618-5
8. Schulz R.B., Rossignoli P., Correr C.J. Fernández-Llimós F., de Toni P.M. [Validation of the short form of the Spanish hypertension quality of life questionnaire (MINICHAL) for Portuguese (Brazil)] // *Arq. Bras. Cardiol.* 2008 Feb; 90 (2): 127-31. [Article in En, Portuguese] PMID: 18392385. DOI: 10.1590/s0066-782x2008000200010
9. Adherencetolong-termtherapies: Evidence for action. Geneva, WHO, 2003. – 198 p. <https://apps.who.int/iris/bitstream/handle/10665/42682/9241545992.pdf;jsessionid=678C598AB5AACF9A679D72B9BB5F4EF1?sequence=1>
10. Bardage C., Isacson D. Hypertension and health related quality of life: an epidemiological study in Sweden // *J. Clin. Epidemiol.* 2001 Feb; 54(2): 172-81. PMID: 11166533. DOI: 10.1016/s0895-4356(00)00293-6
11. Barnason S., Zimmermann L., Anderson A., Mohr-Burt S, Nieveen J. Functional status outcomes of patients with a coronary artery by pass graft over time // *Heart Lung.* 2000 Jan-Feb; 29(1): 33-46. PMID: 10636955. DOI: 10.1016/s0147-9563(00)90035-9
12. Battersby C., Hartley K., Fletcher A., Markowe HJ, Styles W, Sapper H, Bulpitt CJ. Quality of the life in treated hypertension: a cause-control community based study // *J. Hum. Hypertens.* 1995 Dec01; 9(12): 981-6. PMID: 8746643. <https://europepmc.org/article/med/8746643>
13. Baroletti S., Dell’Orfano H. Medication adherence in cardiovascular disease // *Circulation.* 2010 Mar 30; 121(12): 1455-8. PMID: 20351303. DOI: 10.1161/CIRCULATIONAHA.109.904003
14. Deeks A., Lombard C., Michelmore J., Teede H. The effects of gender and age on health related behaviors // *BMC Public Health.* 2009; 9: article 213. <https://bmcpublihealth.biomedcentral.com/articles/10.1186/1471-2458-9-213>
15. Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC) // *Journal of Hypertension.* 2013 Jul; 31(7): 1281-1357. PMID: 23817082. DOI: 10.1097/01.hjh.0000431740.32696.cc
16. Gee M.E., Bienek A., McAlister F.A., Robitaille C., Jofres M., Tremblay M.S., Johansen H., Campbell N.R.C. Factors associated with lack of awareness and uncontrolled high blood pressure among Canadian adults with hypertension // *Can. J. Cardiol.* 2012 May; 28(3): 375-82. PMID: 22402028. DOI: 10.1016/j.cjca.2011.12.012
17. Gu Q., Burt V.L., Paulose-Ram R., Dillon C.F. Gender differences in hypertension treatment, drug utilization patterns, and blood pressure control among US adults with hypertension: data from the National Health and Nutrition Examination Survey 1999-2004 // *Am. J. Hypertens.* 2008 Jul; 21(7): 789-98. PMID: 18451806. DOI: 10.1038/ajh.2008.185
18. Gu Q., Paulose-Ram R., Dillon C., Burt V. Antihypertensive medication seamong US adults with hypertension // *Circulation.* 2006 Jan 17; 113(2): 213-21. PMID: 16391156. DOI: 10.1161/CIRCULATIONAHA.105.542290
19. Ooi H.H.L., Coleman P.L., Duggan J., O’Meara Y.M. Treatment of hypertension in the elderly // *Current Opinion in Nephrology and Hypertension* 1997; 6 (5): 504-9.
20. Ostchega Y., Dillon C.F., Hughes J.P., Carroll M., Yoon S. Trends in hypertension prevalence, awareness, treatment, and control in older U.S. adults: data from the National Health and Nutrition Examination Survey 1988 to 2004 // *J. Am. Geriatr. Soc.* 2007 Jul; 55(7): 1056-65. PMID: 17608879. DOI: 10.1111/j.1532-5415.2007.01215.x
21. Roca-Cusachs A., Ametlla J., Calero S. Comas O., Fernández M., Lospaus R., Monmany J., Morera R., Muñoz M., Peris A. [Quality of life in arterial hypertension] // *Med. Clin. (Barc).* 1992 Apr 4; 98(13): 486-90. [Article in Spanish]. PMID: 1583946
22. Roca-Cusachs A., Dalfó A., Badia X., Aristegui I., Roset M. Relation between clinical and therapeutic variables and quality of life in hypertension // *J. Hypertens.* 2001 Oct; 19(10): 1913-9. PMID: 11593114. DOI: 10.1097/00004872-200110000-00028
23. Sang Hui Chu, Ji Won Baek, Eun Sook Kimetal. Gender Differences in Hypertension Control Among Older Korean Adults: Korean Social Life, Health, and Aging Project // *J. Prev. Med. Public Health.* 2015 Jan; 48(1): 38-47. PMID: 25652709. doi: 10.3961/jpmph.14.043
24. Stokes G.S. Management of hypertension in the elderly patients // *Clin. Interv. Aging.* 2009 Oct 12; 4: 379-89. PMID: 19851513. doi: 10.2147/cia.s5242
25. Zamorano J., Rodriguez P., Cosin J. Hernandez A., Gutierrez-Chico J.L., de Isla L Pérez, Aristegui R., Masramon X., CORONARIA Study Group. Amlodipine reduces predicted risk of coronary heart disease in high-risk patients with hypertension in Spain (The CORONARIA Study) // *J. Int. Med. Res.* 2008 Nov-Dec; 36 (6): 1399-417. PMID: 19094452. DOI: 10.1177/147323000803600630

## ЗМІНИ ПОКАЗНИКІВ ЯКОСТІ ЖИТТЯ ЗАЛЕЖНО ВІД СТУПЕНЯ АРТЕРІАЛЬНОЇ ГІПЕРТЕНЗІЇ В ГЕНДЕРНОМУ АСПЕКТІ

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**Актуальність.** Артеріальна гіпертензія є одним з найпоширеніших хронічних захворювань, для яких в даний час метою терапії є не стільки одужання, скільки поліпшення функції кровообігу при задовільній якості життя.

**Мета:** визначення впливу різних ступенів артеріальної гіпертензії на показники якості життя у пацієнтів жіночої та чоловічої статі.

**Матеріали та методи.** Обстежено 126 пацієнтів на артеріальну гіпертензію, серед яких було 86 жінок (68%), 40 чоловіків (32%) у віці від 40 до 81 років (середній вік  $61,9 \pm 0,3$  років). Артеріальну гіпертензію I ступеня мали 19 осіб (15,1%), II ступеня – 65 пацієнтів (51,6%), III ступеня – 42 особи (33,3%). Контрольну групу склали 43 практично здорових особи, які за демографічними показниками не відрізнялися від основної групи. Анкетування хворих щодо оцінки якості життя проводилось за допомогою опитувальника SF-36 (Short Form-36) при кожному візиті. Показники якості життя оцінювалися в балах.

**Результати.** При аналізі показників якості життя в групі здорових виявлено, що у чоловіків рівень якості життя значно вище, ніж у здорових жінок: «тілесний біль», «рольове функціонування» –  $P1-P2 > 0,5$ ; «фізичне функціонування» –  $P1-P2 < 0,001$ ; «фізичне здоров'я» –  $P1-P2 > 0,5$ , за винятком шкали «загальне здоров'я» –  $P1-P2 < 0,05$  ( $77,2 \pm 3,02$  проти  $63,75 \pm 2,81$ ).

При порівнянні показників якості життя хворих з артеріальною гіпертензією I ступеня і хворих з артеріальною гіпертензією III ступеня достовірні відмінності виявлені за шкалами «життєва сила» ( $P1-P3 < 0,001$ ), та «соціальне функціонування» ( $P1-P3 < 0,5$ ). У хворих же II і III ступенів артеріальної гіпертензії показники якості життя були невисокими самі по собі і розрізнялися за шкалою «рольове функціонування» опитувальника: «життєва сила» ( $P2-P3 > 0,5$ ); УФ ( $P2-P3 > 0,5$ ); «рольове функціонування» ( $P2-P3 < 0,5$ ); «психічне здоров'я» ( $P2-P3 > 0,5$ ).

У пацієнтів з артеріальною гіпертензією I ступеня в порівнянні з артеріальною гіпертензією II ступеня достовірно більш високі показники якості життя по шкалах «життєва сила» ( $80,0 \pm 3,93$  балів) та «рольове функціонування» ( $77,1 \pm 4,04$  балів), але знижені показники «соціальне функціонування» та «психічне здоров'я» ( $48,7 \pm 7,35$  та  $47,41 \pm 2,39$  балів, відповідно).

У хворих з артеріальною гіпертензією I ступеня і III ступеня достовірні відмінності виявлені по шкалах «життєва сила» ( $P1-P3 < 0,001$ ) та «соціальне функціонування» ( $P1-P3 < 0,5$ ); а у пацієнтів з артеріальною гіпертензією II та III ступенів спостерігається суттєве зниження усіх показників якості життя, особливо по шкалах «соціальне функціонування» та «психічне здоров'я» (до  $31,5 \pm 5,19$  та до  $40,31 \pm 2,23$  балів, відповідно).

У пацієнтів з артеріальною гіпертензією I ступеня знижувалися загальне здоров'я ( $87,1 \pm 3,16$ ), фізичне функціонування ( $82,6 \pm 2,86$ ) та тілесний біль ( $87,1 \pm 3,16$ ) балів. У пацієнтів з артеріальною гіпертензією II ступеня спостерігалось суттєве зниження рольового функціонування ( $32,4 \pm 5,19$ ), тілесного болю та загального здоров'я ( $36,0 \pm 6,12$  та  $42,26 \pm 2,68$  балів, відповідно).

**Висновки.** Артеріальна гіпертензія суттєво впливає на якість життя. Фізична активність хворих на артеріальну гіпертензію значно обмежена станом їх здоров'я.

**Ключові слова:** артеріальна гіпертензія, якість життя, гендерний аспект, опитувальник SF-36.

## ИЗМЕНЕНИЯ ПОКАЗАТЕЛЕЙ КАЧЕСТВА ЖИЗНИ В ЗАВИСИМОСТИ ОТ СТЕПЕНИ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ В ГЕНДЕРНОМ АСПЕКТЕ

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**Актуальность.** Артериальная гипертензия является одним из самых распространенных хронических заболеваний, для которых в настоящее время целью терапии является не столько выздоровления, сколько улучшение функции кровообращения при удовлетворительном качестве жизни.

**Цель:** определение влияния различных степеней артериальной гипертензии на показатели качества жизни у пациентов женского и мужского пола.

**Материалы и методы.** Обследовано 126 пациентов с артериальной гипертензией, среди которых было 86 женщин (68%), 40 мужчин (32%) в возрасте от 40 до 81 лет (средний возраст  $61,9 \pm 0,3$  лет). Артериальная гипертензия I степени имели 19 человек (15,1%), II степени – 65 (51,6%), III степени – 42 (33,3%). Контрольную группу составили 43 практически здоровых человека, по демографическим показателям не отличались от основной группы. Анкетирование больных по оценке качества жизни проводилось с помощью опросника SF-36 (Short Form-36) при каждом визите. Показатели качества жизни оценивались в баллах.

**Результаты.** При анализе показателей качества жизни в группе здоровых обнаружено, что у мужчин уровень качества жизни значительно выше, чем у здоровых женщин: «телесная боль», «ролевое функционирование» –  $P1-P2 > 0,5$ ; «физическое функционирование» –  $P1-P2 < 0,001$ ; «физическое здоровье» –  $P1-P2 > 0,5$ , за исключением шкалы «общее здоровье» –  $P1-P2 < 0,05$  ( $77,2 \pm 3,02$  против  $63,75 \pm 2,81$ ).

При сравнении показателей качества жизни больных с артериальной гипертензией I степени и больных с артериальной гипертензией III степени достоверные различия выявлены по шкалам «жизненная сила» ( $P1-P3 < 0,001$ ), и «социальное функционирование» ( $P1-P3 < 0,5$ ). У больных же II и III степеней артериальной гипертензии показатели качества жизни были невысокими сами по себе и различались по шкале «ролевое функционирование» опросника: «жизненная сила» ( $P2-P3 > 0,5$ ); УФ ( $P2-P3 > 0,5$ ); «ролевое функционирование» ( $P2-P3 < 0,5$ ); «психическое здоровье» ( $P2-P3 > 0,5$ ).

У пациентов с артериальной гипертензией I степени по сравнению с артериальной гипертензией II степени достоверно более высокие показатели качества жизни по шкалам «жизненная сила» ( $80,0 \pm 3,93$  баллов) и «ролевое функционирование» ( $77,1 \pm 4,04$  баллов), но снижены показатели «социальное функционирование» и «психическое здоровье» ( $48,7 \pm 7,35$  и  $47,41 \pm 2,39$  баллов, соответственно).

У больных с артериальной гипертензией I степени и III степени достоверные различия выявлены по шкалам «жизненная сила» ( $P1-P3 < 0,001$ ) и «социальное функционирование» ( $P1-P3 < 0,5$ ); а у пациентов с артериальной гипертензией II и III степеней наблюдается существенное снижение всех показателей качества жизни, особенно по шкалам «социальное функционирование» и «психическое здоровье» (до  $31,5 \pm 5,19$  и до  $40,31 \pm 2,23$  баллов, соответственно).

У пациентов с артериальной гипертензией I степени снижались общее здоровье ( $87,1 \pm 3,16$ ), физическое функционирование ( $82,6 \pm 2,86$ ) и телесную боль ( $87,1 \pm 3,16$ ) баллов. У пациентов с артериальной гипертензией II степени наблюдалось существенное снижение ролевого функционирования ( $32,4 \pm 5,19$ ), телесной боли и общего здоровья ( $36,0 \pm 6,12$  и  $42,26 \pm 2,68$  баллов, соответственно).

**Выводы.** Артериальная гипертензия существенно влияет на качество жизни. Физическая активность больных артериальной гипертензией значительно ограничена состоянием их здоровья.

**Ключевые слова:** артериальная гипертензия, качество жизни, гендерный аспект, опросник SF-36.

## EARLY COMPLEX REHABILITATION TREATMENT OF PATIENTS WITH FRACTURE OF DISTAL METAEPIPHYSIS OF THE RADIUS

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**Relevance.** Fractures of the distal metaepiphysis of the radial bone among all fractures range from 11% to 30%. Unsatisfactory results of treatment in patients over 70 years old are found in 44% of cases. Timely and adequate rehabilitation treatment is important for obtaining good results in the treatment of such patients.

**Objective:** to improve the results of treatment of patients with fractures of the distal metaepiphysis of the radial bone based on early comprehensive individual rehabilitation treatment.

**Materials and methods.** 97 patients with displaced fractures of the distal metaepiphysis of the radius were observed. Among them, 67 are women (69.1%), over 50 years old – 64 (66%). Used conservative treatment with a sparing technique of one-stage reduction. Upon completion of the correction, according to the indications, measures were prescribed for the prevention of neurodystrophic syndrome, depending on the likelihood of its development (according to the temperature gradient of the fingers of the extremities) in the form of drug therapy. Massage, kinesiotherapy and physiotherapy began on the second day. The pain intensity was determined using a visual analogue scale. The nature of pain was determined by the DN4 questionnaire (questionnaire for the diagnosis of neuropathic pain). For subjective unified assessment of hand function in the long term after hand injury, I used a specific questionnaire DASH (Disability of the Arm, Shoulder and Hand Outcome Measure) – a questionnaire of outcomes and disability of the hand and hand.

**Results.** Rehabilitation treatment at admission and at the early outpatient stage was complex, individual, taking into account the periods of illness. The debris correction was painless, low-traumatic, rational fixing bandages were used. The volume of drug therapy was determined by the value of the temperature gradient of the fingers.

**Conclusion.** The proposed method for the rehabilitation of patients with fractures of the distal metaepiphysis of the radius is highly effective: good and satisfactory (according to the DASH scale) results were obtained in 97.8% of cases, unsatisfactory – in 2.2%.

**Key words:** fracture of the distal metaepiphysis of the radius, rehabilitation treatment.

**Relevance.** Fracture of the distal metaepiphysis of the radial bone (FDMERB) occurs quite often [2, 7], among all fractures they range from 11% to 30% [3, 6]. A high proportion among this group of victims are women in the postmenopausal period, with low bone mineral density [4, 5]. Unsatisfactory results of treatment in patients over 70 years old are found in 44% of cases [4, 6].

Timely and adequate rehabilitation treatment is important for obtaining good results in the treatment of patients with fractures of the distal metaepiphysis of the radius.

**Objective** of the work is to improve the results of treatment of patients with fractures of the distal metaepiphysis of the radial bone based on early comprehensive individual rehabilitation treatment.

### MATERIALS AND METHODS

To achieve this goal, it was necessary to solve such problems.

1. To determine the likelihood of developing post-traumatic neurodystrophic syndrome according to generally accepted predictors and T gradient.

2. To formulate the scope of early rehabilitation treatment in patients with fractures of the distal metaepiphysis of the radius.

3. To justify and conduct an individual complex of rehabilitation treatment using rational fixation of fragments, drug therapy, physiotherapy and kinesiotherapy.

4. To determine the effectiveness of the proposed complex treatment.

Under our supervision there were 97 patients with displaced FDMERB fractures. They were treated conservatively. Women prevailed – 67 observations (69.1%), over 50 – 64 (66%). In conservative treatment, in 28 patients with extra-articular stable FDMERB, a sparing technique of simultaneous reduction was used, in which, with a fixed elbow joint, traction was performed along the length and flexion towards the existing displacement. At the same time, the doctor eliminated the displacement in width by pressing the fingers on the distal fragment, after which the angular displacement was corrected by palmar flexion.

A visual analogue scale (VAS) was used to determine the severity of pain. The nature of pain was determined by the DN4 questionnaire (questionnaire for the diagnosis of neuropathic pain).

The instruction was given to the patient to evaluate his feelings according to the following principles. On a scale of 10 cm (100 mm) the level of pain intensity is

marked with a dot. The starting point denotes the absence of pain – 0, followed by mild pain, moderate pain, severe pain and the end point - unbearable pain – 10. Although it seems primitive, the VAS has wide application in clinical practice and is universally recognized by clinicians.

For a subjective unified assessment of hand function in the long term after hand injury, a specific DASH questionnaire (Disability of the Arm, Shoulder and Hand Outcome Measure) was used – a questionnaire of outcomes and disability of the hand and arm. In 2005, he underwent the process of intercultural adaptation in Russian, and the Russian version is available on the website of the Institute of Labor and Health (Canada) [9]. The main section of the DASH (Disability/Symptom Scale) questionnaire consists of 30 question items related to the state of hand function over the past week. Each item has 5 answer options, scored from 1 to 5. The sum of the points for all items is then converted to a 100-point scale.

DASH rates upper limb disability from 0 - no disability (good functionality) to 100 - excessive disability [8].

## RESULTS AND DISCUSSION

In all observations during the first three days in patients with fractures of the radius in a typical place, the pain syndrome had a neuropathic character (varying degrees of severity). This was due to anatomical predisposition. The carpal tunnel is a narrow tunnel formed by the bones of the wrist and the transverse wrist ligament [1]. Median nerve neuropathy with ray fractures in a typical location consists in trauma and compression of the median nerve in the canal cavity.

It is generally accepted that the predisposing factors in the development of post-traumatic neurodystrophic syndrome are vascular diseases, premorbid degenerative changes in muscle-tendon-periarticular tissues, osteochondrosis of the cervical spine, diabetes mellitus. Most of the victims had this pathology.

Complete multimodal analgesia was very important in the prevention of the development of post-traumatic neurodystrophic syndrome at the initial stages. This was achieved by the following methods.

A 2% solution of lidocaine 15-20 ml was injected into the hematoma of the fracture, reduction was performed no earlier than 5 minutes later. Non-steroidal anti-inflammatory drugs were used (intramuscular injection of Dexamol 15-20 minutes before install). Later, in the acute period (up to 3-7 days), patients received tablet forms.

Auxiliary therapy included the use of calcium and vitamin D3 preparations (Calcium D3 Nycomed, 1 tablet 2 times a day for 30 days), B vitamins (Neurobion, Duovit), alpha-lipoic acid antioxidants (Berlition) or Actovegin. The obligatory component was the use of the Keltican polypeptide. A drug containing cytidine monophosphate and uridine monophosphate is indicated for the treatment of neuropathic pain with lesions of the peripheral nervous system. It improves axonal and neuronal regeneration. He was taken 1 tablet 3 times a day for 2-3 weeks. In order to reduce muscle tone, the muscle relaxant medocalm was used. A long-term, damper, with increasing effort, traction of fragments was performed.

Upon completion of the correction, according to the indications, measures were prescribed to prevent neurodystrophic syndrome (NDS), depending on the likelihood of its development (according to the temperature gradient of the fingers of the extremities (Fig. 1, Table 1).

For further immobilization, plaster casts were most often used. However, although they have a number of advantages and are most widely used in everyday practice, they are not without drawbacks. They are not very hygienic; they do not fix the fragments firmly enough. Therefore, in 32 cases we used modern plastic bandages made of hard polymer plaster Scotchcast.

Table 1

The amount of preventive treatment taking into account the temperature gradient

Gradient T, °C	Probability of NDS development	Scope of preventive treatment
0,4±0,09°C	small	Anesthetic therapy Dexketoprofen, Vitamins of group B and C, Ca and Vitamin D3, polypeptides (Keltikan).
1,3±0,1°C	average	Pain therapy Dexketoprofen, Vitamins of group B and C, Ca and Vitamin D3, polypeptides (Keltikan), muscle relaxants (Mydocalm), antioxidants alpha-lipoic acid (Berlition), Solcoseryl, Actovegin.
1,9±0,1°C	high	Anesthetic therapy Dexketoprofen, Vitamins B and C, Ca and Vitamin D3, polypeptides (Keltikan), muscle relaxants (Midocalm), antioxidants alpha lipoic acid (Berlition), Solcoseryl, Actovegin, anticonvulsants Gabapentin – 300 mg at night or Pregabalin (Lyrics) – 150 mg/day, decongestants Troxevasin 900 mg/day and Lioton 1000 ointment.
2,2±0,5°C	inevitable occurrence	Pain therapy Dexketoprofen, Vitamins B and C, Ca and Vitamin D3, polypeptides (Keltican), muscle relaxants (Midocalm), antioxidants alpha lipoic acid (Berlition), Solcoseryl, Actovegin, anticonvulsants Gabapentin – 300 mg per night Lyrica) – 150 mg/day, decongestants Troxevasin 900 mg/day and Lioton 1000 ointment.

Note: NDS – neurodystrophic syndrome



Fig. 1. Carrying out thermometry with a thermometer Thermofocus 01500A3

Strips of plaster were glued to the skin of the fingers longitudinally, threads were laid on them. The latter are fixed with circular bandages. Thus, the traction force is evenly distributed over the entire surface of 1-2-3 fingers. Traction does not cause painful sensations; patients are assessed by patients at  $3.8 \pm 0.09$  points on the VAS scale (easily tolerated pain).

Rough manipulations were not performed. After matching the fragments in the position of slight stretching and slight flexion or extension of the hand, the fragments were fixed with plastic or plaster (if it was impossible to use plastic) bandages. After 2 weeks, if necessary, a staged removal of the hand to the mid-physiological position was carried out. After 4-6 weeks, after X-ray control, the bandage was removed, and further active rehabilitation treatment was carried out.

A short bandage from Scotchcast to the metacarpophalangeal joints holds the fracture of the distal metacarpus of the radius well and makes it possible to move the fingers from the first day.

The objectives of medical physical culture in the first immobilization period were: general strengthening and psychoemotional tonic effect on the body; improvement

of blood circulation and tissue trophism; prevention of muscle atrophy and joint contracture.

To solve these problems, certain complexes of physical therapy were used. The specific gravity of the exercises was as follows. About 75% were exercises for other segments of the musculoskeletal system, movements in the joints of the injured limb free from immobilization, and breathing exercises. Self-care exercises with a healthy hand were included.

Exercises for the injured hand accounted for about 25%, first in isometric and physiological modes, passive and then active exercises for the fingers began. Physiotherapy exercises for the 1st finger were carried out separately – its withdrawal simultaneously with extension of 1-4 fingers, flexion in the metacarpophalangeal and interphalangeal joints. Attention was drawn to the condition of the fixation bandage in this area – the hole was sufficient for free movement, the edges did not injure the skin. The appearance of significant pain and pronounced edema indicated an excessive load; tolerable pain and slight swelling – about the optimal load. Figure 2 shows a diagram of a set of exercises proposed by Dobyns JH, 1975, modified and widely used by other authors (Strafun S.S., 2015, Timoshenko S.V., 2010 Vinnik A.V., 2016 Naumenko L.Yu., 2012 ) for FDMERB fractures from the early stages.

Straight 2-4 fingers were bent in the metacarpophalangeal joints, at the same time the unbent 1 finger was brought to them. Subsequently, with unbent metacarpophalangeal joints, signal-extension movements in the interphalangeal joints were performed, the exercise ended by squeezing the fingers of the injured limb into a fist. The exercise was accompanied by raising the extended arm vertically upward, lying or standing. When bending the fingers, a soft rubber ball or foam sponge was used as a countermeasure.

After removing the fixation bandage, kinesiotherapy was performed in the second (postimmobilization) period. Its peculiarity was the change in the proportion of general strengthening exercises up to 25%. At the same time, 75% were special exercises for the injured hand. The tasks of physical therapy at this stage were:

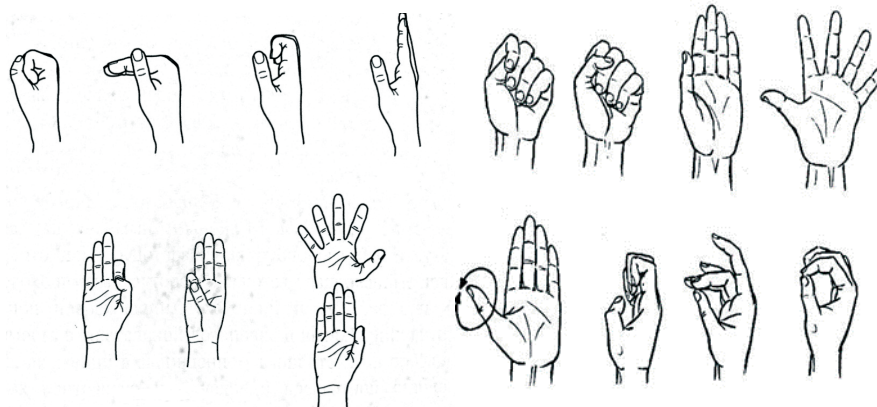


Fig. 2. Scheme of a set of exercises proposed by Dobyns J.H., 1975

restoration of the function of the injured hand, mobility in the joints; elimination of muscle atrophy.

For this, the following kinesiotherapy means were intended. General developmental and breathing exercises were carried out individually, with and without sports equipment. In the first days after removing the gauze bandage, both passive and passive-active movements were used for the injured hand; active for all joints with a gradual increase in the range of motion and dosage of each exercise.

Immediately after the end of immobilization, gymnastics was performed for the wrist, elbow and shoulder joints. Exercises for the wrist joint included the following exercises: active flexion, extension, radial and ulnar bone deviation, as well as rotational movements of the hand and forearm. Began exercises «stretching» – rapprochement of bent and unbend brushes with increasing efforts. In the future, they began to perform exercises with the resistance of the healthy hand or the hand of the methodologist, exercises with resistance (using an elastic rubber bandage or expander), stretching exercises. Exercise in young patients with weights or with apparatus gave good functional results.

The task of kinesiotherapy in this period is the complete restoration of the impaired hand function. Household and labor rehabilitation was carried out. The proportion of elements of occupational therapy increased. Exercises were prescribed and performed that imitated actions in everyday life and in the process of work (turning on the light, hammering nails, opening doors, lacing, bulkheading small objects, brushing teeth, etc.).

Games were used that restored muscle strength, movement in joints, and coordination.

In case of FDMERB fractures, massage was prescribed from 2-3 days after the injury, after the acute inflammatory processes subsided. During the period of immobilization of the forearm with a plaster or plastic bandage, massage of the upper-thoracic reflex-segmental areas was used, as well as massage of the damaged upper limb – shoulder and hand – stroking, rubbing and kneading the raised arm; massage of the entire healthy symmetrical limb using all massage techniques. The massage was performed in kinesiotherapy.

In the second and third periods, massage of the para-vertebral zone and the injured limb is continued. First, the segments above the fracture were massaged – shoulder girdle, shoulder, then the damaged area – forearm and

distal part – hand. Forearm massage was performed as follows. First, stroking and rubbing of soft tissues was performed, then longitudinal, lumbar kneading of the muscles, stretching and compression at a fast pace. All methods of intensive massage at the site of the fracture were alternated with stroking. The massage ended with general stroking of the injured limb and active movements.

In the first period, patients with FDMERB used ultraviolet irradiation, Peiler-therapy with the Bioptron device (Fig. 3), longitudinal calcium electrophoresis, UHF, magnetotherapy.

In the second, post-immobilization, period, they sought to restore the full range of motion in the joints, restore the strength and endurance of the arm muscles. We expanded the range of physiotherapeutic agents. Physiotherapy treatment is aimed at creating a background, facilitates the conduct of kinesiotherapy. To eliminate residual trophic disorders, microwave therapy, magnetotherapy, darsonvalization, laser therapy, Peiler-therapy were used. We used phonophoresis – ultrasound at a dosage of 0.6-0.8 watts/cm<sup>2</sup> with Fastum gel and Lyoton 1000.



Fig. 3. Peiler-therapy with the Bioptron apparatus.

In cases of persistent dysfunction of the hand, repeated courses were prescribed using therapeutic mud and hydrotherapy – radon or hydrogen sulfide baths; prescribed sanatorium treatment.

Studies of the results of rehabilitation treatment of patients with FDMERB fractures show the following. Multimodal anesthesia, differentiated and reasonably applied drug therapy, sparing reduction, early kinesiotherapy made it possible to eliminate pain syndrome by day 7 in the vast majority of victims. Rehabilitation treatment included painless correction of



Fig. 4. Functional result of treatment of a fracture of the distal metaepiphysis of the radius.

displaced fragments, rational fixation dressings, early kinesiotherapy, massage, and physiotherapy.

The functional results of treatment of patients with FDMERB fractures according to the DASH scale indicate the following. Good and satisfactory results were obtained in 97.8%, with 2.2% of cases being unsatisfactory. Clinical observation is shown in Figure 4.

This testifies to the high efficiency of the use of complex rehabilitation: rational low-traumatic correction and fixation of fragments; individual drug therapy, determined using the method of predicting the likelihood of developing post-traumatic stress (temperature gradient) and conducting early kinesiotherapy, massage and physiotherapy, taking into account the period of treatment and individual characteristics.

## CONCLUSIONS

The proposed method of rehabilitation of patients with FDMERB fractures is highly effective: good and satisfactory (on the DASH scale) results were obtained in 97.8% of cases, unsatisfactory – in 2.2%.

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## REFERENCES

1. Al-Zamil M.Kh. [Carpal syndrome] // Clinical neurology. 2008; 1: 41-5. [In Russian]. <https://elibrary.ru/item.asp?id=13759213>
2. Buryanov A.A. [Post-traumatic dystrophy of the extremities (Sudeck's syndrome). Questions of pathogenesis, diagnosis and treatment] [Author's abstract dissertation cand. med. sciences]. Kharkov, 1990: 24 p. [In Russian]
3. Danilov A.B., Davydov O.S. [Diagnostic scales for assessing neuropathic pain] // Pain. 2007; 3(16): 11-5. [In Russian] <https://elibrary.ru/item.asp?id=9563486>
4. Yepanov V.V. [Clinical and epidemiological characteristics of fractures of the distal radius due to osteoporosis in the Far North (for example, the city of Yakutsk)] [Author's abstract dissertation Cand. med. sciences]. Yakutsk, 2006: 22 p. [In Russian]
5. Korzh N.A., Kotulsky I.V. [Pathogenesis of post-traumatic pain syndromes of extremities] // International medical journal. 2002; 1-2: 134-7. [In Russian]
6. Golubev V.L., Merkulova D.M., Orlova O.R., Danilov A.B. [Tunnel hand syndromes] // Russian medical journal. 2009; 17(10): 22-6. [In Russian] [https://www.rmj.ru/articles/bolevoy\\_sindrom/Tunnelynye\\_sindromy\\_ruki/](https://www.rmj.ru/articles/bolevoy_sindrom/Tunnelynye_sindromy_ruki/)
7. Akimova T.N., Savchenko V.V., Gladkova E.V., Kolmykova A.S., Chibrikov A.G. [Average terms of temporary disability in patients with long bone fractures] // Trauma. 2009; 10(1): 44-7. [In Russian] <http://www.mif-ua.com/archive/article/20088>
8. [Subjective assessment of the function of the upper limb]. [In Russian] <https://sites.google.com/site/71microsurgery/vopros-vracu/dash>
9. DASH: Disability of the Arm, Shoulder and Hand Outcome Measure. [www.dash.iwh.on.ca](http://www.dash.iwh.on.ca)

## РАНІС КОМПЛЕКСНЕ РЕАБІЛІТАЦІЙНЕ ЛІКУВАННЯ ХВОРИХ З ПЕРЕЛОМОМ ДИСТАЛЬНОГО МЕТАЕПІФИЗА ПРОМЕНЕВОЇ КІСТКИ

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**Актуальність.** Переломи дистального метаепіфіза променевої кістки серед всіх переломів складають від 11 % до 30 %. Незадовільні результати лікування у пацієнтів старше 70 років зустрічаються в 44 % випадків. Важливим для отримання хороших результатів при лікуванні таких хворих є своєчасне і адекватне реабілітаційне лікування.

**Мета:** покращити результати лікування хворих з переломами дистального метаепіфіза променевої кістки на основі раннього комплексного індивідуального реабілітаційного лікування.

**Матеріали та методи.** Спостерігали 97 постраждалих з переломами дистального метаепіфіза променевої кістки зі зміщенням. Серед них 67 жінок (69,1 %), старше 50 років – 64 (66 %). Використовували консервативне лікування з делікатною технікою одномоментного вправлення. По завершенні корекції за показаннями призначалася заходи щодо профілактики нейродистрофічного синдрому в залежності від ймовірності його розвитку (за даними градієнта температури пальців кінцівок) у вигляді медикаментозної терапії. Масаж, кінезотерапію і фізіолікування починали з другого дня. Сила болю визначалася за візуально-аналоговою шкалою. Характер болю визначався опитувальником DN4 (опитувальник для діагностики нейропатичного болю). Для суб'єктивної уніфікованої оцінки функції кисті в віддалені терміни після травми кисті використовували специфічний опитувальник DASH (Disability of the Arm, Shoulder and Hand Outcome Measure) - опитувальник результатів і нездатності руки і кисті.

**Результати.** Реабілітаційне лікування при надходженні і на ранньому амбулаторному етапі було комплексним, індивідуальним, з урахуванням періодів хвороби. Корекція уламків була безболісна, малотравматична, використовувалися раціональні фіксуючі пов'язки. Обсяг медикаментозної терапії визначався за значенням градієнта температури пальців.

**Висновок.** Запропонований метод реабілітації хворих з переломами дистального метаепіфіза променевої кістки є високоефективним: хороші й задовільні (за шкалою DASH) результати отримані в 97,8 % випадків, незадовільні – в 2,2 %.

**Ключові слова:** перелом дистального метаепіфіза променевої кістки, реабілітаційне лікування

**РАННЕЕ КОМПЛЕКСНОЕ РЕАБИЛИТАЦИОННОЕ ЛЕЧЕНИЕ БОЛЬНЫХ С ПЕРЕЛОМOM  
ДИСТАЛЬНОГО МЕТАЭПИФИЗА ЛУЧЕВОЙ КОСТИ**

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**Актуальность.** Переломы дистального метаэпифиза лучевой кости среди всех переломов составляют от 11 % до 30 %. Неудовлетворительные результаты лечения у пациентов старше 70 лет встречаются в 44 % случаев. Важным для получения хороших результатов при лечении таких больных является своевременное и адекватное реабилитационное лечение.

**Цель:** улучшить результаты лечения больных с переломами дистального метаэпифиза лучевой кости на основе раннего комплексного индивидуального реабилитационного лечения.

**Материалы и методы.** Наблюдали 97 пострадавших с переломами дистального метаэпифиза лучевой кости со смещением. Среди них 67 женщин (69,1 %), старше 50 лет – 64 (66 %). Использовали консервативное лечение с шадящей техникой одномоментного вправления. По завершении коррекции по показаниям назначалась мера по профилактике нейродистрофического синдрома в зависимости от вероятности его развития (по данным градиента температуры пальцев конечностей) в виде медикаментозной терапии. Массаж, кинезотерапию и физиолечение начинали со второго дня. Сила боли определялась по визуальной-аналоговой шкале. Характер боли определялся опросником DN4 (опросник для диагностики нейропатической боли). Для субъективной унифицированной оценки функции кисти в отдаленные сроки после травмы кисти использовали специфический опросник DASH (Disability of the Arm, Shoulder and Hand Outcome Measure) – опросник исходов и неспособности руки и кисти.

**Результаты.** Реабилитационное лечение при поступлении и на раннем амбулаторном этапе было комплексным, индивидуальным, с учетом периодов болезни. Коррекция обломков была безболезненна, малотравматична, использовались рациональные фиксирующие повязки. Объем медикаментозной терапии определялся по значению градиента температуры пальцев.

**Вывод.** Предложенный метод реабилитации больных с переломами дистального метаэпифиза лучевой кости является высокоэффективным: хорошие и удовлетворительные (по шкале DASH) результаты получены в 97,8 % случаев, неудовлетворительные – в 2,2 %.

**Ключевые слова:** перелом дистального метаэпифиза лучевой кости, реабилитационное лечение.

## THE EVOLUTION IN THE TREATMENT OF PEPTIC ULCER AND ITS COMPLICATIONS

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**Relevance.** Duodenal ulcer is complicated by perforation in 5-15% of patients. The priority area of abdominal surgery is the introduction of minimally invasive methods. Laparoscopic surgeries are becoming an alternative to standard technologies.

**Objective:** to analyze the effectiveness of open and laparoscopic palliative and conditionally radical surgical interventions in patients with perforated duodenal ulcer in the early and late two-year periods.

**Materials and methods.** The efficacy of open and laparoscopic palliative and conditionally radical surgical interventions was studied in 181 patients with perforated duodenal ulcer in the early and late two-year periods. The patients were divided into two groups: 92 patients who underwent laparoscopic surgery and 89 patients who underwent open surgery. The groups are comparable in age, time from the onset of the disease, and the diameter of the ulcer. After the operation, the intensity of pain was assessed in points using a visual analogue scale, the rate of healing. Complications in the early postoperative period were analyzed (wound suppuration, pneumonia, extrasystole, atrial fibrillation, abscesses, suture failure). Analyzed the development of peritonitis and its characteristics (serous-fibrinous, fibrinous-purulent; local, general).

**Results.** Laparoscopic operations take less time than open ones. In the first four days after surgery, the average pain score was significantly lower ( $p<0.05$ ) in patients after minimally invasive surgery. There was a tendency towards earlier activation of patients in the group of laparoscopic operations. The duration of hospital stay after laparoscopic operations averaged  $5.11\pm 0.08$  days (from 3 to 7 days) and was significantly less ( $p<0.05$ ) for that in patients who underwent open surgery. The two-year cumulative incidence of ulcer recurrence in the group of laparoscopic operations was 16.3% (15 patients), in the group of open operations - 19.1% (17 patients).

**Conclusions.** Laparoscopic palliative and conditionally radical surgeries in patients with perforated ulcer have advantages in the early postoperative period, which is associated with minor pain syndrome and earlier activation of patients and, as a consequence, a decrease in the length of hospital stay. In the long-term two-year postoperative period, the results of palliative and conditionally radical operations in the laparoscopic and open versions did not differ significantly.

**Key words:** ulcer, perforation, laparoscopic treatment.

**Relevance.** For more than a century of development, surgery of peptic ulcer disease has passed a complex and controversial path. In the history of this section, stages can be distinguished that differed in the technical possibilities of surgical treatment and in the goal set by the surgeons, depending on the views on the etiology and pathogenesis of peptic ulcer that reigned at that time.

The first period – from the 80s of the XIX to the 20s of the XX century, the method of choice is gastroenterology. The second period – 30-60 years of the XX century, the method of choice – gastric resection. The third period – 70-90 years of the XX century – the rapid development of organ-preserving methods, vagotomy led to the expansion of the arsenal of surgical interventions and the use of the principle of individual choice of treatment method «each patient has his own operation» [1].

The successes achieved in the 80-90s of the twentieth century in the study of the pathogenesis of peptic ulcer disease associated with the discovery of the role of

*Helicobacter pylori* (HP) and the introduction into clinical practice of new antiulcer drugs (different generations of proton pump blockers) made it possible to reconsider the principle of treatment of peptic ulcer disease, to prefer a therapeutic method of treatment.

At the same time, there has been a steady tendency towards a decrease in the number of planned surgical interventions for duodenal ulcer (DU).

However, the use of modern advances in pharmacotherapy did not contribute to a decrease in the incidence of complications in gastroduodenal ulcers; therefore, there is still little hope for a significant reduction in the number of patients with breakthrough ulcers [4, 5]. The course of peptic ulcer disease is complicated by perforation in 5-15% of patients, which is 1.6-3.4% in the structure of acute surgical diseases of the abdominal organs [2, 3].

One of the priority directions in the development of modern abdominal surgery is the development and implementation of minimally invasive methods of

surgical interventions. Laparoscopic operations are becoming an alternative to standard technologies and occupy a certain place in the surgery of perforated duodenal ulcer. The low invasiveness of the method makes it possible not only to save the patient's life, but also predetermines the comfortable course of the postoperative period, a high cosmetic effect, and rapid physical and social rehabilitation of patients [6, 7].

**Objective.** To analyze the effectiveness of open and laparoscopic palliative and conditionally radical surgical interventions in patients with perforated duodenal ulcer in the early and late two-year periods.

## MATERIALS AND METHODS

The analysis of the treatment of 181 patients with perforated duodenal ulcer was carried out. All patients were divided into two groups, according to the method of performing the surgery. The first group consisted of 92 patients who underwent palliative (suturing of the perforated hole) or conditionally radical (excision of an ulcer with duodenoplasty) laparoscopic operations (LO group), the second group – 89 patients who underwent similar operations in an «open» way (OO group).

The studied groups were comparable in terms of the main indicators. The average age of patients in the LO group was  $36.2 \pm 1.0$  years, in the OO group –  $35.1 \pm 1.1$  years ( $p=0.502$ ). In both groups, there were significantly more men than women, 91.3% (LO) and 88.76% (OO), respectively.

The groups also did not differ significantly in the time elapsed from the onset of the disease to surgery. In patients of the LO group, it was  $6.91 \pm 0.18$  hours, in patients of the OO group –  $6.65 \pm 1.19$  hours,  $p=0.316$ .

In both groups, serous-fibrinous peritonitis was more often observed, less often fibrinous-purulent (Table 1).

Local and general peritonitis occurred with approximately the same frequency. There were no

statistically significant differences between the groups in the nature of peritonitis and its prevalence,  $p=0.947$ .

The diameter of the ulcer defect in patients of both groups ranged from 3 mm to 15 mm: in the LO group, on average,  $6.24 \pm 0.23$  mm; in the OO group –  $6.18 \pm 0.22$  mm,  $p=0.85$ .

After surgery, the intensity of pain was assessed in points using a visual analogue scale.

## RESULTS AND ITS DISCUSSION

Analysis of the immediate results showed that laparoscopic palliative operations require less time compared to open ones. Thus, in patients of the LO group, the average duration of surgery was  $57.8 \pm 1.9$  min (from 25 min to 100 min), and in the OO group –  $83.2 \pm 1.7$  min (from 45 min to 120 min),  $p=0.001$ . This reduction in the time of surgical intervention is primarily due to the absence of the stage of suturing the anterior abdominal wall.

In the early postoperative period, patients reported pain in the area of surgery of varying intensity. In the first four days after surgery, the pain intensity was assessed in points using a visual analogue scale. On the first day after surgery, there were no patients in one of the groups who were not worried about pain. At the same time, it should be noted that after laparoscopic interventions pain with an intensity of 5-6 points (severe) was only in 14 (15.2%) patients, and after open interventions – in 42 (47.2%) patients. While weak and tolerant (2-4 points) was found in 78 (84.8%) patients in the LO group versus 47 (52.8%) patients in the OO group,  $p<0.05$ . In the following days of the postoperative period, a decrease in the intensity of pain was observed in both groups. On the 4th day, no pain or mild pain (0-2 points) was noted in 67 (72.8%) patients in the LO group and 32 (36.0%) in the OO group,  $p<0.05$ .

Table 2

Complications in the early postoperative period

Complications	Group LO		Group OO		Total		P
	abs.	%	abs.	%	abs.	%	
Suppuration of the wound	3	3,3	4	4,5	7	3,9	0,667
Pneumonia	2	2,2	4	4,5	6	3,3	0,383
Extrasystole, Atrial fibrillation	3	3,3	2	2,2	5	2,8	0,677
Abscesses	0	0,0	1	1,1	1	0,6	0,308
Failure of seams	1	1,1	0	0,0	1	0,6	0,324

Notes: LO – laparoscopic operations; OO – operations in an «open» way.

Table 1

Distribution of patients in groups by the nature of peritoneal exudate

The nature of the exudate	Group LO		Group OO		Total	
	abs.	%	abs.	%	abs.	%
Serous	34	37,0	31	34,8	65	35,9
serous fibrinous	54	58,7	54	60,7	108	59,7
fibrinous-purulent	4	4,3	4	4,5	8	4,4
Total	92	100	89	100	181	100

Notes: LO – laparoscopic operations; OO – operations in an «open» way.

The lower intensity of postoperative pain in the patients of the LO group contributed to the earlier activation of the patients in comparison with the OO group, which, as is known, is the prevention of thromboembolic, pulmonary and cardiovascular complications.

It should be noted that although there were no significant differences in terms of recovery of bowel function between the groups ( $p=0.068$ ), on the third day the motor-evacuation activity of the intestine recovered in 63 (68.5%) patients after laparoscopic operations, and in 52 (58.4%) after open operations. Resumption of food intake was directly related to the timing of recovery of intestinal motility and was also statistically similar in the groups.

In the early postoperative period, a number of patients in both groups were diagnosed with complications, the list of which is given in Table 2.

The duration of hospital stay after laparoscopic operations averaged  $5.11 \pm 0.08$  days (from 3 days to 7 days) and was significantly less than that in patients who underwent open surgery –  $7.55 \pm 0.11$  days (from 5 days to 12 days),  $p < 0.001$ . This fact can be explained by the earlier activation of patients in the LO group and a slight pain syndrome in most of them, equally with patients in the OO group.

Long-term results of surgical treatment of patients were followed by us for up to two years. During this time, 11 patients dropped out of the total number of patients at different times and for various reasons (not related to peptic ulcer disease and surgery) – 6 from the LO group and 5 from the OO group. We considered the results of the examination of these patients as censored data. Ulcer recurrence occurred in 32 (17.7%) patients. The two-year cumulative incidence of ulcer recurrence in the LO group was 16.3% (15 patients), in the OO group – 19.1% (17 patients), there was no significant difference in the results between the groups ( $p=0.628$ ). The main reason for relapse was discontinuation of antiulcer therapy. The largest absolute increase in the frequency of recurrence of peptic ulcer disease occurred in the period from 7 to 12 months, the smallest - in the interval 19-24 months.

## CONCLUSIONS

1. Laparoscopic palliative and conditionally radical surgeries in patients with perforated ulcer have

advantages in the early postoperative period, which is associated with minor pain syndrome and earlier activation of patients and, as a consequence, a decrease in the length of hospital stay.

2. In the long-term two-year postoperative period, the results of palliative and conditionally radical operations in the laparoscopic and open versions did not differ significantly.

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## REFERENCES

- Balalykin D.A. [The history of the development of surgical treatment of gastric ulcer and duodenal ulcer in Russia (late XIX - XX centuries)] // *Surgery*. 2001; 3: 64-6. [in Russian]. <http://stati3452.narod.ru/gaster/17.pdf>
- Borisov A.E., Mitin S.E., Peshekhonov S.I. [et al.] [Laparoscopic suturing of perforated gastroduodenal ulcers] // *Endoscopic surgery*. 2000; 2: 12-3. [in Russian].
- Afendulov S.A., Zhuravlev G.Yu., Kadirov K.M. [Rehabilitation of patients after suturing a perforated gastroduodenal ulcer] // *Scientific medical journal Avicenna Bulletin*. 2011; 4: 25-8. [in Russian]. <https://cyberleninka.ru/article/n/reabilitatsiya-bolnyh-posle-ushivaniya-perforativnoy-gastroduodenalnoy-yazvy/viewer>
- Satsukevich V.N. [Surgical treatment of perforated gastroduodenal ulcers] // *Surgery*. 2001; 5: 24-7. [in Russian]. <http://stati3452.narod.ru/gaster/23.pdf>
- Fomin PD, Povch OA. [Modern view on the problem of treatment of perforated gastroduodenal ulcers] // *Collection Science works of Shupika KMAPE*. Kyiv, 2001; 10 (4): 399-405. [in Ukrainian].
- Minutolo V., Gagliano G., Rinzivillo C., Minutolo O., Carnazza M., Racalbutto A., Dipietro S., Destri G.L. Laparoscopic surgical treatment of perforated duodenal ulcer // *Chirurgia Italiana*. 2009 May-Jun; 61(3): 309-13. PMID: 19694232. <https://pubmed.ncbi.nlm.nih.gov/19694232/>
- Karimian F., Aminian A., Lebaschi A.H., Mirsharifi R., Alibakhshi A. Perforated Peptic Ulcer, Comparison Between Laparoscopic and Open Repair // *Shiraz E-Medical Journal*. 2008; 10(1): 20-6. <https://sites.kowsarpub.com/semj/articles/73128.html>

## ЕВОЛЮЦІЯ В ЛІКУВАННІ ВИРАЗКОВОЇ ХВОРОБИ ТА ЇЇ УСКЛАДНЕНЬ

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**Актуальність.** Виразкова хвороба дванадцятипалої кишки ускладнюється перфорацією у 5-15 % хворих. Пріоритетним напрямком абдомінальної хірургії є впровадження малоінвазивних методів. Лапароскопічні операції стають альтернативою стандартним технологіям.

**Ціль:** проаналізувати ефективність відкритих та лапароскопічних паліативних і умовно радикальних оперативних втручань у хворих з перфоративною виразкою дванадцятипалої кишки в ранньому та віддаленому дворічному періодах.

**Матеріали та методи.** Вивчено ефективність відкритих та лапароскопічних паліативних і умовно радикальних оперативних втручань у 181 хворого з перфоративною виразкою дванадцятипалої кишки в ранньому та віддаленому дворічному періодах. Пацієнти були розділені на дві групи: 92 пацієнта, яким виконувалися лапароскопічні операції та 89 хворих, яким операція виконувалася відкритим способом. Групи співставні за віком, часом від початку захворювання, діаметром виразкового дефекту. Після операції оцінювали інтенсивність болю в балах за візуально-аналоговою шкалою, швидкість загоєння. Аналізували ускладнення в ранньому післяопераційному періоді (нагноєння рани, пневмонія, екстрасистоля, миготлива аритмія, абсцеси, неспроможність швів). Аналізували розвиток перитоніту та його характеристики (серозно-фібринозний, фібринозно-гнійний; місцевий, загальний).

**Результати.** Лапароскопічні операції потребують меншого часу порівняно з відкритими. У перші чотири доби після операції середній бал болю був достовірно нижчим ( $p < 0,05$ ) у хворих після малоінвазивних операцій. Відмічена тенденція до більш ранньої активізації пацієнтів групи лапароскопічних операцій. Тривалість перебування хворих у стаціонарі після лапароскопічних операцій складала в середньому  $5,11 \pm 0,08$  доби (від 3 до 7 діб) і була достовірно меншою ( $p < 0,05$ ) за таку у хворих, що перенесли відкриті операції. Дворічна кумулятивна частота рецидиву виразки в групі лапароскопічних операцій склала 16,3 % (15 хворих), в групі відкритих операцій – 19,1 % (17 хворих).

**Висновки.** Лапароскопічні паліативні і умовно-радикальні операції у хворих з перфоративною виразкою мають переваги в ранньому післяопераційному періоді, що пов'язано з незначним больовим синдромом та більш ранньою активізацією пацієнтів і, як наслідок, зменшенням тривалості перебування у стаціонарі. У віддаленому дворічному післяопераційному періоді результати паліативних і умовно-радикальних операцій в лапароскопічному і відкритому варіанті суттєво не відрізнялись.

**Ключові слова:** виразка, перфорація, лапароскопічне лікування.

## ЭВОЛЮЦИЯ В ЛЕЧЕНИИ ЯЗВЕННОЙ БОЛЕЗНИ И ЕЕ ОСЛОЖНЕНИЙ

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**Актуальность.** Язвенная болезнь двенадцатиперстной кишки осложняется перфорацией у 5-15% больных. Приоритетным направлением абдоминальной хирургии является внедрение малоинвазивных методов. Лапароскопические операции становятся альтернативой стандартным технологиям.

**Цель:** проанализировать эффективность открытых и лапароскопических паллиативных и условно радикальных оперативных вмешательств у больных с перфоративной язвой двенадцатиперстной кишки в раннем и отдаленном двухлетнем периодах.

**Материалы и методы.** Изучена эффективность открытых и лапароскопических паллиативных и условно радикальных оперативных вмешательств у 181 больного с перфоративной язвой двенадцатиперстной кишки в раннем и отдаленном двухлетнем периодах. Пациенты были разделены на две группы: 92 пациента, которым выполнялись лапароскопические операции и 89 больных, которым операция выполнялась открытым способом. Группы сопоставимыми по возрасту, времени от начала заболевания, диаметру язвенного дефекта. После операции оценивали интенсивность боли в баллах по визуально-аналоговой шкале, скорость заживления. Анализировали осложнения в раннем послеоперационном периоде (нагноение раны, пневмония, экстрасистолия, мерцательная аритмия, абсцессы, несостоятельность швов). Анализировали развитие перитонита и его характеристики (серозно-фибринозный, фибринозно-гнойный; местный, общий).

**Результаты.** Лапароскопические операции требуют меньше времени по сравнению с открытыми. В первые четверо суток после операции средний балл боли был достоверно ниже ( $p < 0,05$ ) у больных после малоинвазивных операций. Отмечена тенденция к более ранней активизации пациентов группы лапароскопических операций. Продолжительность пребывания больных в стационаре после лапароскопических операций составляла в среднем  $5,11 \pm 0,08$  суток (от 3 до 7 суток) и была достоверно меньше ( $p < 0,05$ ) таковой у больных, перенесших открытые операции. Двухлетняя частота рецидива язвы в группе лапароскопических операций составила 16,3 % (15 больных), в группе открытых операций – 19,1% (17 больных).

**Выводы.** Лапароскопические паллиативные и условно-радикальные операции у больных с перфоративной язвой имеют преимущества в раннем послеоперационном периоде, что связано с незначительным болевым синдромом и более ранней активизацией пациентов и, как следствие, уменьшением продолжительности пребывания в стационаре. В отдаленном двухлетнем послеоперационном периоде результаты паллиативных и условно-радикальных операций в лапароскопическом и открытом варианте существенно не отличались.

**Ключевые слова:** язва, перфорация, лапароскопическое лечение.

## PECULIARITIES OF USING ORTHODONTIC ACTIVATORS FOR DISTAL BITE AND APPLICATION OF RETENTION APPARATUS TO RETAIN RESULTS

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**Relevance.** Distal occlusion is accompanied by certain morphological, functional and aesthetic changes, in which there are disorders of external respiration, speech disorders, dysfunction of chewing and swallowing. Today the problem of treatment of occlusion anomalies is not completely solved. The presence of errors and complications in the treatment of distal occlusion, the presence of recurrence of the disease in the form of a double occlusion, which necessitates repeated, and often unsuccessful treatment, indicates that the problem is still far from its final solution.

**Objective:** to investigate the effectiveness of the use of orthodontic activators for the treatment of distal occlusion and retention devices to maintain the results of treatment.

**Materials and methods.** 126 children aged 9-12 years with distal occlusion are divided into 2 groups. Group I (n=63) – children with distal occlusion and physiological type of respiration; Group II (n=63) – children with distal occlusion and pathological (oral) type of breathing. Conducted clinical, myographic and anthropometric studies. All patients were treated by wearing a removable functional two-jaw orthodontic activator for at least 16 hours a day, with mandatory use during sleep, for 6 months. In addition to this hardware method of treatment, preventive measures were prescribed: myogymnastic and breathing exercises. Correction of orthodontic activator was performed once a month. A control electromyographic study to determine the effectiveness of treatment was performed 3 months after the start of treatment (selectively, in some patients - also in the sixth month of treatment). Nylon floss, to keep the teeth in the achieved position.

**Results.** The study of the designs of retention devices and comparison of their effectiveness showed that after active orthodontic treatment the most effective retention can be achieved by using a retainer made of flex wire and nylon thread impregnated with liquid photopolymer. The most optimal way to fix the fixed retention apparatus was as follows: complete completion of the active period of treatment; control of fissure-tubercle contact; professional teeth cleaning; conducting X-ray control to identify the position of the roots of the teeth; production of gypsum models and their fixation in the occluder; detection of contact points of the frontal group of teeth; detection of the location of the retainer in the oral cavity; making a retainer indirectly; fixation of the retention apparatus in the oral cavity. Our proposed method of manufacturing and fixing non-removable retainers with the use of nylon thread allows to achieve reliable long-term retention of the achieved positive results after active orthodontic treatment.

Analysis of the study data of children aged 9-12 years with distal occlusion and pathological (oral) type of respiration compared with the control group showed an increase in all measured EMG parameters for the temporalis muscles (in the range of 16-31.1±3.12%) and reduction - for the actual masticatory and circular muscles of the mouth (in the range of 17.0-29.8±3.09% and 16.8-35.9%, respectively). The total deviation of the values of the obtained indicators from the normative ranges from 16.0 to 35.9 ±2.56%. These abnormalities can be seen as a manifestation of the formation of a pathological muscle reaction, accompanied by negative changes in the appearance of the patient.

The design of a removable functionally acting two maxillary orthodontic activator for simultaneous treatment of distal occlusion and dysfunction of masticatory and facial muscles in children with physiological and pathological types of respiration has been developed. It consists of a monoblock and a vestibular plate, monolithically connected to each other.

**Conclusions.** In patients with distal occlusion, treatment with a removable functional two-jaw orthodontic activator helps to restore myodynamic balance in the dental system, resulting in improved patient facial expression, self-esteem and quality of life. Wearing non-removable retainers with the use of nylon thread allows to achieve reliable long-term retention of the achieved positive results after active orthodontic treatment.

**Key words:** distal occlusion, retention apparatus, two-jaw orthodontic activator.

**Relevance.** Bite anomalies are manifested by local and general disorders of the body, reflected in the development of adjacent organs and the entire body as a whole. The distal occlusion is accompanied by certain morphological, functional and aesthetic changes [1], such as: a decrease in the volume of the nasal cavities, impaired

pneumatization of the airway sinuses of the skull and impaired dynamic balance of the muscles of the perioral region and tongue, in which a number of functions of the child suffer, namely, functional impairments external respiration, speech impairment, impaired chewing and swallowing.

Today, through the efforts of many specialists, including Ukrainian ones, certain successes have been achieved in the orthodontic treatment of certain forms of distal occlusion [2, 3]. The number of successfully completed cases of distal occlusion treatment ranges from 30% to 80% [4]. However, the presence of errors and complications in the treatment of distal occlusion, the presence of relapses of the disease in the form of a double bite, which necessitates repeated, and often unsuccessful treatment, indicates that the problem is still far from its final solution. Obviously, there is a need for an integrated approach to the prevention and treatment of distal occlusion, which would include measures aimed at overcoming both the dentofacial anomaly and dysfunctions of the masticatory and facial muscles, since these two pathologies are inherently linked not only in the process of prevention and treatment, but also in the process of human life in general, and therefore need simultaneous action. Forming a correct bite in a child will ensure its healthy development and improve the quality of life in general.

After the end of the active period of treatment, the retention period begins, which is the final stage of orthodontic treatment. Most often in this period, retainers are used, including removable and non-removable.

The retention period can last from several months to several years, or lifelong. The duration of retention after the completion of orthodontic treatment depends on the period of occlusion formation, the use of functional or mechanical treatment methods, the presence of eliminated functional disorders and the achieved treatment results [3]. Each case requires an individual approach, since retention depends on many factors: the age of the patient, the initial clinical situation, the degree of rotation of the subglacial anomaly, the treatment plan (with or without the removal of individual teeth), the timing of the active period of treatment, the neatness of the patient, the design features of the orthodontic apparatus, creation of functional occlusion upon completion of treatment, the presence of bad habits.

A non-removable retainer is fixed to the dental composite material to the inner surface of the teeth, usually canine to canine. At the same time, the design, as a rule, is inconspicuous, durable, comfortable, the patient quickly gets used to it. There are many other designs, but there are no clear guidelines for their use.

Given the variety of clinical forms and manifestations of distal occlusion, not the last place among the problematic issues of dentoalveolar anomalies is its diagnosis, which is based on the etiological factor of the occurrence of distal occlusion. To correctly diagnose occlusion anomalies, orthodontists have adopted a problem-oriented approach developed in medicine that allows them to view the patient as a whole. With this approach, each factor is assessed that may be part of the etiology of the anomaly, may affect it directly or the results of its treatment. After all, the dentoalveolar

apparatus functions due to the complex interaction of teeth, periodontium and jaws, masticatory and facial muscles, muscles of the tongue, temporomandibular joint and ligamentous apparatus, vascular and nervous system [5, 6].

Among a number of factors that cause the formation of distal occlusion is heredity. A survey of 1,609 Finnish children showed a high incidence of hereditary anomalies of the dental apparatus and confirmed the widespread view that hereditary factors determine the development of jaws and occlusion, while external factors have only a modifying effect. It is believed that 17-21% of anomalies of the dental apparatus, including occlusion, are genetically determined by hereditary factors, the rest - acquired as a result of adverse environmental factors. Based on the use of clinical and genealogical method, pedigrees and segregation analysis of families of probands with dental anomalies, the vertical distribution of prognostic occlusion in both sexes was revealed. Prognathic occlusion has an autosomal dominant and multifactorial type of inheritance. The influence of blood marriages on the structure of the pathology of the dental apparatus, which in prognathic occlusion is manifested in 36.6%. The population and intrafamilial (excluding inbreeding) frequencies of prognostic occlusion are, respectively, 10% and 15%. And the intrafamilial inbreeding rate in families with occlusal anomalies is 8.25 times higher than its average population values. This type of information makes it possible to conduct qualified medical and genetic counseling, as a result of which patients or their relatives receive information about the inheritance of the pathology, the likelihood of its development and ways to prevent it. There are data on the autosomal dominant type of inheritance of diastema, trem, crowding of teeth, anomalies in the position of individual teeth, anomalies in the number of teeth. Prognathia has a multifactorial and autosomal dominant type of inheritance, deep bite - multifactorial. It is considered necessary to consult children with occlusal abnormalities in a geneticist [7].

There is a reliable relationship between the frequency of dental anomalies and nasal breathing disorders. Thus, dental anomalies in children with pathology of the nasal cavity and pharynx are 2.2 times more common ( $84.7 \pm 2.7\%$ ) than in children without ENT diseases ( $38.7 \pm 1.9\%$ ;  $p < 0.001$ ). There is a reliable direct link between difficult nasal breathing and narrowing of dental arches, dysto-, mesio- and dysocclusion. Respiratory dysfunction is one of the reasons for unsuccessful treatment and recurrence of occlusal abnormalities.

Distal occlusion has the highest recurrence rate: from 60% in cases with tooth extraction, and 75-100% of recurrence - in clinical situations without tooth extraction [8]. Recurrence after orthodontic treatment is due to the peculiarities of occlusal relationships, genetically determined mismatch in the size and shape of the teeth of the upper and lower jaws, continued growth of the

jaws, myofunctional mismatch due to redistribution of masticatory muscle tone after orthodontic exercise.

**Objective:** to investigate the effectiveness of the use of orthodontic activators for the treatment of distal occlusion and retention devices to maintain the results of treatment.

### MATERIALS AND METHODS

Patients were treated with our patented removable functional double-jaw orthodontic activator (utility model patent № 59838, registered in the State Register of Utility Patents of Ukraine on 25.05.2011). The aim of the proposed utility model is to create a multifunctional, easy to manufacture and use removable functional two-jaw orthodontic activator for effective simultaneous treatment of distal occlusion, regulation of masticatory and facial muscles and restoration (improvement) of nasal breathing. This goal is achieved by creating a removable functional two-jaw orthodontic activator containing a plastic candy bar with a bed for teeth. In this case, according to the utility model, the activator additionally contains a vestibular plate, monolithically connected to a plastic candy bar (Fig. 1, Fig. 2).

After clinical, myographic and anthropometric studies of patients with distal occlusion and physiological type of respiration (group I, n=63) and patients with distal occlusion and pathological type of respiration (group II, n=63), they were prescribed orthodontic treatment by our patented orthodontic activator. In addition to the instrumental method of treatment, preventive measures were prescribed, namely: myogymnastic and breathing exercises.

The orthodontic activator was made individually for each patient in the dental laboratory. During the manufacture, the individual characteristics of each patient were taken into account. Taking into account these features, certain additional elements of the activator were used. Patients were instructed on the rules of wearing the activator, compliance with oral hygiene. It was mandatory to wear the activator for at least 16 hours

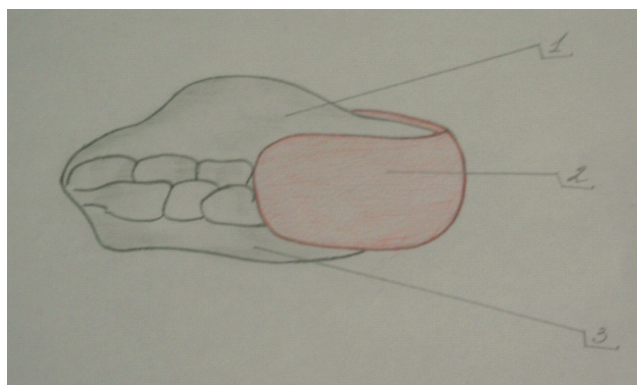


Fig. 1. Scheme of removable functionally operating two-jaw orthodontic activator: 1 – plastic monoblock; 2 – vestibular plate, monolithically connected to the monoblock; 3 – bed for teeth.



Fig. 2. Removable functionally acting double-slotted orthodontic activator:  
a - bottom view, b - front view, c - side view with closed teeth, d - front view with closed teeth

a day with the obligatory use during sleep. Correction of orthodontic activator was performed once a month. A control electromyographic study to determine the effectiveness of treatment in the I and II clinical groups was performed 3 months after the start of treatment, which corresponds to the optimal time of transformation of the usual myotatic reflex. Selectively, some patients were also monitored at the sixth month of treatment.

These features are the essence of a useful model and ensure the achievement of the technical result – the regulation of masticatory and facial muscles, restoration (improvement) of nasal breathing, as well as treatment of distal occlusion. The causal relationship between the essential features of the utility model and the technical result is that the vestibular plate, monolithically connected to the plastic candy bar, when closing the lips causes muscle tension that closes the mouth, which increases and regulates their tone, as well as prevents the passage of air through the mouth, which, in turn, leads to the regulation of nasal breathing.

## RESULTS AND DISCUSSION

Analysis of the data obtained indicates the presence of a clear tendency to improve not only the pathology of the occlusion within the position of the teeth and jaws, but also about significant positive changes in the tone of the masticatory and facial muscles, which lead to an improvement in the function of breathing and swallowing, which is a priority in our study. Particular attention should be paid to improving the function of the circular muscle of the mouth, because it is this anatomical formation that affects the closure of the lips, which, in turn, directly proportionally affects the type of breathing and the patient's appearance and is fundamental in our study.

Orthodontic treatment in general, and in particular, the treatment with the orthodontic activator proposed by us, helps to restore myodynamic balance in the dentoalveolar system, as a result of which the patient's facial expression changes for the better and, as a result, the patient's self-esteem improves, and his quality of life improves. Children become more organized, they do better in school, orthodontic treatment provides a psychotherapeutic effect and, therefore, has social significance [9].

Timely and correct implementation of preventive measures contributes to the acceleration of orthodontic

treatment, reduces the likelihood of recurrence of the disease, has a positive effect on the formation and vital activity of the human body as a whole, and in certain periods of the formation of the dentition can contribute to self-elimination of individual anomalies of the dentition.

This goal is achieved by using a removable, functionally acting two jaw orthodontic activator, contains a plastic monoblock with a bed for teeth. Moreover, according to the invention, the activator additionally contains a vestibular plate monolithically connected to a plastic monoblock. The listed features constitute the essence of the useful model and ensure the achievement of the technical result - regulation of the function of the masticatory and facial muscles, restoration (improvement) of the function of nasal breathing, as well as the treatment of distal occlusion.

The vestibular plate, monolithically connected to a plastic monoblock, when the lips are closed, causes tension of the muscles that close the mouth opening, the latter leads to an increase and regulation of their tone, and also makes it impossible for air to pass through the mouth, which, in turn, leads to the regulation of the function of nasal breathing ... The restoration of the reduced and uneven electromyographic parameters of the circular muscle of the mouth was observed by us already 3 months after the start of treatment (Tables 1, 2), confirming the necessity and expediency of the equipment developed and used by us.

The use of a functional apparatus of the activator-bionator type for the maintenance of not only teeth, but also occlusion. At the end of the active period of treatment, the patient should have no sagittal fissure, therefore, the constructive bite for the functional apparatus is established without presenting the lower jaw forward - this is necessary to prevent the recurrence of class II anomalies. Difficulties can arise as a result of inconsistent wearing of a functional device, usually at night, therefore, special design day retainers are required to control the position of the teeth in the first months. A patient with a severe growth problem also needs an additional retainer. Conventional maxillary and mandibular retainers should be correctly used for patients in whom further growth may not cause a relapse; subsequently, these retainers will be replaced with a functional night-wearing apparatus, unless, of course, a tendency towards relapse has not been observed after a few months.

Table 1  
EMG parameters of muscles in patients with distal occlusion and normal breathing and clinical group I - 3 months after the start of treatment

Muscles DMS	Ta, s	Tc, s	k	Ampmax, mV	Ampmean, mV	Teamax	Teamean
m.masseterdex.	0,3064	0,247	1,240	0,347	0,315	312,256	253,860
m.massetersin.	0,3059	0,247	1,238	0,349	0,314	304,020	252,664
m.temporalisdex	0,3302	0,252	1,310	0,608	0,548	316,386	286,235
m.temporalesin	0,3343	0,254	1,314	0,614	0,544	312,894	285,054
m.orbicularisoris	0,3055	0,245	1,248	0,463	0,420	259,484	221,368

Notes: EMG – electromyography; DMS – dental-maxillary system.

**EMG parameters of muscle muscles of patients with distal occlusion and pathological type of respiration of clinical group II - 3 months after the start of treatment**

Muscles DMS	Ta, s	Tc, s	k	Ampmax, mV	Ampmean, mV	Teamax	Teamean
m.masseterdex.	0,271	0,222	1,224	0,316	0,294	270,319	213,261
m.massetersin.	0,272	0,220	1,237	0,314	0,286	276,484	222,039
m.temporalisdex.	0,359	0,274	1,311	0,638	0,581	344,922	310,005
m.temporalessin.	0,368	0,279	1,318	0,646	0,592	335,969	314,115
m.orbicularisoris.	0,263	0,213	1,232	0,419	0,360	224,674	198,710

Notes: EMG – electromyography; DMS – dental-maxillary system.

We have proposed a non-removable retention device [10] to reduce the risk of possible complications during its use, by improving the existing non-removable retainer. This was achieved by using a nylon thread to keep the teeth in the achieved position, maintaining a high level of oral hygiene regardless of the duration of treatment, and also developed indications for the use of this device after the final stage of active orthodontic treatment.

The advantage of our proposed fixed retention orthodontic appliance is that the nylon thread is fixed at 14,13,12,11,21,22,23,24 on the upper and lower jaw using a low viscosity photopolymer composite material.

Nylon thread is a synthetic material, does not dissolve, 1.0 mm in diameter. It is characterized by high wear resistance and mechanical strength, resistance to most solvents.

Capron is soft, has a high tensile strength, is resistant to abrasion, is very flexible, with a smooth surface, and is also physiologically harmless, that is, indifferent.

## CONCLUSIONS

In patients with distal occlusion, treatment with a removable functional two-jaw orthodontic activator helps to restore myodynamic balance in the dental system, resulting in improved patient facial expression, self-esteem and quality of life. Wearing non-removable retainers with the use of nylon thread allows to achieve reliable long-term retention of the achieved positive results after active orthodontic treatment.

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## REFERENCES

1. Khudonogova E.Ya. [Treatment of distal occlusion in patients with disorders of the musculoskeletal system] [dissertation – 14.00.21]. St. Petersburg, 2006. [in Russian]
2. Denga OV, Rajab M., Mirchuk B.N. [Prevention of concomitant complications in the treatment of dentoalveolar anomalies in children with fixed orthodontic appliances] // News of Stomatology. 2004; 2: 63-7. [in Russian]
3. McLaughlin R., Bennett D., Trevisy X. Systematized mechanics of orthodontic treatment / translation from English. Flis P.S. editor. Lviv: GalDent, 2005: 324 p. [in Russian]
4. Garbatsevich D.V. Treatment of distal mixed occlusion with standard and individually made functional devices [dissertation – 14.00.21]. Minsk, 2009. [in Russian] file:///C:/Users/%D0%A2%D0%B0%D1%82%D1%8C%D1%8F%D0%BD%D0%B0%20%D0%98%D0%B2%D0%B0%D0%BD%D0%BE%D0%B2%D0%BD%D0%B0/Downloads/201302281259214939.pdf
5. Mirza A.I. Diagnostics and treatment of pain syndrome of dysfunction of the temporomandibular joint [dissertation – 14.00.22]. Kyiv, 2002: 304 p. [in Russian]
6. Mitke P.P. Errors, relapses, retention, headache in orthodontics // Orthodontics. 2004; 1 (25): 26-9. [in Russian] <http://www.fesmu.ru/elib/Article.aspx?id=109580>
7. Khoroshilkina F.Ya. Modern analysis of classifications of dento-maxillofacial anomalies, planning complex treatment and predicting its results // Dentistry for all. 2004; 4: 36. [in Russian] [https://e-stomatology.ru/prensa/periodika/st\\_d\\_f/4\\_2004/](https://e-stomatology.ru/prensa/periodika/st_d_f/4_2004/)
8. Dubova OM Optimization of the results of orthodontic treatment in adult patients with distal occlusion [dissertation – 14.00.21]. Perm, 2008: 106 p. [in Russian] <https://www.dissercat.com/content/optimizatsiya-rezultatov-ortodonticheskogo-lecheniya-vzroslykh-patsientov-s-distalnoi-okklyu>
9. Flis P.S., Kasyanenko D.M. The need to eliminate etiological factors in the treatment of distal occlusion through interaction with doctors of related specialties // Modern dentistry. 2014; 1: 30-3. [in Russian] <https://cyberleninka.ru/article/n/neobhodimost-ustraneniya-etiological-faktorov-pri-lechenii-distalnogo-prikusa-putem-vzaimodeystviya-s-vrachami-smezhnyh/viewer>
10. Abdullah Annan, Flis P.S. Retention method. Ukraine патент UA 69560. 2012 Apr 25. [in Ukraine]

## ОСОБЛИВОСТІ ВИКОРИСТАННЯ ОРТОДОНТИЧНИХ АКТИВАТОРІВ ДЛЯ ДИСТАЛЬНОГО ПРИКУСУ ТА ЗАСТОСУВАННЯ РЕТЕНЦІЙНИХ АПАРАТІВ ДЛЯ УТРИМАННЯ РЕЗУЛЬТАТІВ ЛІКУВАННЯ

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**Актуальність.** Дистальний прикус супроводжується певними морфологічними, функціональними та естетичними змінами, при яких спостерігаються порушення функції зовнішнього дихання, порушення мовлення, порушення функцій жування та ковтання. Сьогодні не до кінця вирішена проблема лікування аномалій прикусу. Наявність помилок і ускладнень при лікуванні дистального прикусу, наявність рецидивів захворювання у вигляді подвійного прикусу, що викликає необхідність повторного, а нерідко і безуспішного лікування, свідчить, що проблема ще далека від свого остаточного вирішення.

**Ціль:** дослідити ефективність застосування ортодонтичних активаторів для лікування дистального прикусу та ретенційних апаратів для утримання результатів лікування.

**Матеріали та методи.** 126 дітей віком 9-12 років з дистальним прикусом поділені на 2 групи. I група (n=63) – діти з дистальним прикусом та фізіологічним типом дихання; II група (n=63) – діти з дистальним прикусом та патологічним (ротовим) типом дихання. Проводили клінічні, міографічні та антропометричні дослідження. Всі пацієнти проходили лікування шляхом носіння знімного функціонально діючого двохщелепового ортодонтичного активатора менше 16 годин на добу, з обов'язковим застосуванням під час сну, протягом 6 місяців. Додатково до цього апаратного методу лікування були призначені профілактичні заходи: міогімнастичні та дихальні вправи. Корекція ортодонтичного активатора проводилась один раз на місяць. Контрольне електроміографічне дослідження для визначення ефективності лікування проводилось через 3 місяці після початку лікування (вибірково, у деяких пацієнтів – також на шостому місяці лікування). По закінченні активного періоду лікування, для зменшення ризику розвитку можливих ускладнень, нами запропоновано удосконалений незнімний ретенційний апарат, із застосуванням капронової нитки, для утримання зубів в досягнутому положенні.

**Результати.** Вивчення конструкцій ретенційних апаратів та порівняння їх ефективності показало, що після проведеного активного ортодонтичного лікування найбільш ефективної ретенції можна досягти, застосовуючи ретейнер з дроту флекс та з капронової нитки, просоченої рідким фотополімером. Найбільш оптимальний спосіб фіксації незнімного ретенційного апарату полягав у наступному: повне завершення активного періоду лікування; проведення контролю фісурно-бугоркового контакту; професійне чищення зубів; проведення рентген-контролю для виявлення положення коренів зубів; виготовлення гіпсових моделей та фіксація їх в оклюдаторі; виявлення точок контакту фронтальної групи зубів; виявлення місця розташування ретейнера в ротовій порожнині; виготовлення ретейнера непрямым способом; фіксація ретенційного апарату в ротовій порожнині. Запропонований нами спосіб виготовлення і фіксації незнімних ретейнерів із застосуванням капронової нитки дозволяє домогтися надійної довгострокової ретенції досягнутих позитивних результатів після активного ортодонтичного лікування.

Аналіз даних дослідження дітей віком 9-12 років з дистальним прикусом та патологічним (ротовим) типом дихання порівняно з контрольною групою показав підвищення всіх вимірюваних ЕМГ-параметрів для скроневих м'язів (в межах 16-31,1±3,12 %) і зниження – для власне жувальних та колового м'язу рота (в межах 17,0-29,8±3,09 % і 16,8-35,9 %, відповідно). Загальне відхилення значень отриманих показників від нормативного коливається в межах 16,0-35,9±2,56 %. Дані відхилення можуть бути розцінені як прояв формування патологічної реакції м'язів, що супроводжується негативними змінами у зовнішньому вигляді пацієнта.

Розроблено конструкцію знімного функціонально діючого двохщелепового ортодонтичного активатора для одночасного лікування дистального прикусу та порушень функції жувальної та мимічної мускулатури у дітей з фізіологічним та патологічним типами дихання. Він складається з моноблоку та вестибулярної пластинки, монолітно з'єднаних між собою.

**Висновки.** У пацієнтів з дистальним прикусом лікування знімним функціонально діючим двохщелеповим ортодонтичним активатором сприяє відновленню міодинамічної рівноваги в зубощелеповій системі, в результаті покращуються вираз обличчя пацієнта, його самооцінка і якість життя. Носіння незнімних ретейнерів із застосуванням капронової нитки дозволяє домогтися надійної довгострокової ретенції досягнутих позитивних результатів після активного ортодонтичного лікування.

**Ключові слова:** дистальний прикус, ретенційний апарат, двохщелеповий ортодонтичний активатор

## ОСОБЕННОСТИ ИСПОЛЬЗОВАНИЯ ОРТОДОНТИЧЕСКИХ АКТИВАТОРОВ ДЛЯ ДИСТАЛЬНОГО ПРИКУСА И ПРИМЕНЕНИЕ РЕТЕНЦИОННЫХ АППАРАТОВ ДЛЯ УДЕРЖАНИЯ РЕЗУЛЬТАТОВ ЛЕЧЕНИЯ

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**Актуальность.** Дистальный прикус сопровождается определенными морфологическими, функциональными и эстетическими изменениями, при которых наблюдаются нарушения функции внешнего дыхания, нарушение речи, нарушение функции жевания и глотания. Сегодня не до конца решена проблема лечения аномалий прикуса. Наличие ошибок и осложнений при лечении дистального прикуса, наличие рецидивов заболевания в виде двойного прикуса, что вызывает необходимость повторного, а нередко и безуспешного лечения, свидетельствует, что проблема еще далека от своего окончательного решения.

**Цель:** исследовать эффективность применения ортодонтических активаторов для лечения дистального прикуса и ретенционных аппаратов для удержания результатов лечения.

**Материалы и методы.** 126 детей в возрасте 9-12 лет с дистальным прикусом разделены на 2 группы. I группа (n = 63) - дети с дистальным прикусом и физиологическим типом дыхания; II группа (n = 63) - дети с дистальным прикусом и патологическим (ротовым) типом дыхания. Проводили клинические, миографические и антропометрические исследования. Все пациенты проходили лечение путем ношения съемного функционально действующего двухчелюстного ортодонтического активатора не менее 16 часов в сутки, с обязательным применением во время сна в течение 6 месяцев. Вдобавок к этому аппаратному методу лечения были назначены профилактические мероприятия: миогимнастические и дыхательные упражнения. Коррекция ортодонтического активатора проводилась один раз в месяц. Контрольное электромиографическое исследование для определения эффективности лечения проводилось через 3 месяца после начала лечения (выборочно, у некоторых пациентов - также на шестом месяце лечения). По окончании активного периода лечения, для уменьшения риска развития возможных осложнений, нами предложен усовершенствованный несъемный ретенционный аппарат, с применением капроновой нити, для удержания зубов в достигнутом положении.

**Результаты.** Изучение конструкций ретенционных аппаратов и сравнение их эффективности показало, что после проведенного активного ортодонтического лечения наиболее эффективной ретенции можно достичь, применяя ретейнер из проволоки флекс и из капроновой нити, пропитанной жидким фотополимером. Наиболее оптимальный способ фиксации несъемного ретенционного аппарата заключался в следующем: полное завершение активного периода лечения; проведения контроля физио-бугоркового контакта; профессиональная чистка зубов; проведения рентген-контроля для выявления положения корней зубов; изготовление гипсовых моделей и фиксация их в окклюдаторе; выявление точек контакта фронтальной группы зубов; выявление местоположения ретейнера в ротовой полости; изготовление ретейнера непрямым способом; фиксация ретенционного аппарата в ротовой полости. Предложенный нами способ изготовления и фиксации несъемных ретейнеров с применением капроновой нити позволяет добиться надежной долгосрочной ретенции достигнутых положительных результатов после активного ортодонтического лечения.

Анализ данных исследования детей 9-12 лет с дистальным прикусом и патологическим (ротовым) типом дыхания по сравнению с контрольной группой показал повышение всех измеряемых ЭМГ-параметров для височных мышц (в пределах 16-31,1 ± 3,12%) и снижение - для собственно жевательных и круговой мышцы рта (в пределах 17,0-29,8 ± 3,09% и 16,8-35,9% соответственно). Общее отклонение значений полученных показателей от нормативного колеблется в пределах 16,0-35,9 ± 2,56%. Данные отклонения могут быть расценены как проявление формирования патологической реакции мышц, сопровождающееся негативными изменениями во внешнем виде пациента.

Разработана конструкция съемного функционально действующего двухчелюстного ортодонтического активатора для одновременного лечения дистального прикуса и нарушений функции жевательной и мимической мускулатуры у детей с физиологическим и патологическим типами дыхания. Он состоит из моноблока и вестибулярной пластинки, монолитно соединенных между собой.

**Выводы.** У пациентов с дистальным прикусом лечение съемным функционально действующим двухчелюстным ортодонтическим активатором способствует восстановлению миодинамического равновесия в зубочелюстной системе, в результате улучшаются выражение лица пациента, его самооценка и качество жизни. Ношение несъемных ретейнера с применением капроновой нити позволяет добиться надежной долгосрочной ретенции достигнутых положительных результатов после активного ортодонтического лечения.

**Ключевые слова:** дистальный прикус, ретенционный аппарат, двухчелюстной ортодонтический активатор.

## FORENSIC MEDICAL AND LEGAL ASPECTS OF THE PROVISION OF MEDICAL CARE IN OBSTETRICS AND GYNECOLOGY

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**Relevance.** Sometimes statistics on medical errors are hushed up, and information about individual incidents becomes known thanks to the media.

**Objective:** to identify the most common obstetric-gynecological profile defects and their causes by analyzing the data of the State Statistics Service on maternal and infant mortality during pregnancy, childbirth and the postpartum period and compare it with the forensic analysis of obstetric-gynecological profile medical care.

**Materials and methods.** 625 cases were analyzed according to the State Statistics Service on maternal and infant mortality during pregnancy, childbirth and the postpartum period, court sentences in criminal cases under Articles 139 and 140 of the Criminal Code of Ukraine, according to the Unified State Register of Court Decisions of Ukraine since 2009 in 2019, as well as data from forensic medical examination commissions on “medicinal matters” for 2013-2019 performed by the State Institution “Main Bureau of Forensic Medical Examination of the Ministry of Health of Ukraine”, including cases of previous departmental audits by the commissions of the Health Administration. The data obtained were subjected to statistical processing by standard methods of descriptive statistics.

**Results.** In these 255 examinations, defects in the provision of medical care were found by expert commissions in 186 cases, which amounted to 72.9%. Moreover, of these «defective cases», 62.9% (117 cases) were in a direct causal relationship with an unfavorable outcome; 35.5% (6 cases) - in some deficiencies that did not have a causal relationship with the onset of fetal death. In 3 cases of examinations in gynecology, there were contradictions in the entries in the medical documentation, they did not allow assessing the quality of medical care and the relationship with the consequences. At the pre-hospital stage (in the clinic), defects were allowed in 65.5%, and at the hospital - in 72.8%. In the presence of departmental inspections in 23%, there was a complete coincidence of the results of the conclusions of the commissions of the bureau of forensic medical examination and medical examination, and only in cases of significant defects in direct causal connection with the consequences. At the same time, when analyzing 53 court sentences according to the register of court decisions, it turned out that 13 of them related to the obstetric and gynecological profile, and 12 of them were indictment. In all cases, the source of evidence in cases was exclusively the “Expert Conclusions”.

**Conclusions.** It was found that forensic medical examinations for the provision of obstetric and gynecological medical care occupy a leading place in the overall structure of commission examinations in “medical matters”, in the vast majority of examinations, defects in the provision of medical care were found that were in direct causal connection with an unfavorable outcome.

**Key words:** forensic medical examination, obstetrics, gynecology, defect, provision of medical care.

**Relevance.** The problem of so-called «medical errors» is relevant even in highly developed countries. For example, in 1999, the US Institute of Medicine published a report entitled «To Err Is Human», which announced that up to 98,000 Americans die each year from medical errors [1]. However, despite the measures taken by Congress (systematic courses and training for medical staff, strengthening control over the work of physicians through the establishment of special commissions), in 2019 medical errors remained just as common. Among the WHO findings: About 10% of hospitalized patients worldwide suffer from nosocomial infections. Medical errors occur in approximately 40% of primary and outpatient patients. Diagnostic and treatment errors are detrimental to millions and cost billions of dollars each year. According to researchers at Johns Hopkins University, 250,000 Americans die each year from medical errors, although no official statistics are available. In Ukraine, official statistics on medical errors are silenced, and information about individual incidents becomes known through the media [4, 5, 6]. It is a clear

fact that such errors are common in those areas of medical practice that are associated with emergency surgery, such as obstetrics and gynecology, surgery, anesthesiology [7]. While in Europe and America the issue of correctness of medical care is solved by doctors of a certain specialty and lawyers [8], in Ukraine these issues are dealt with by forensic experts, which is emphasized by our legislation [9, 10, 11].

However, in the presence of a complaint from relatives or other persons about poor quality treatment to the Ministry of Health, departmental inspections are carried out, where the commission of doctors of the Health Departments (HD) determines the correctness of medical care in a particular case. Only in the presence of a complaint to law enforcement agencies is a forensic medical examination appointed in the framework of criminal proceedings under Articles 139 and 140 of the Criminal Code of Ukraine. In order to accurately assess the correctness of medical care, in particular, obstetrics and gynecology, which is the most common among

these examinations, it is necessary to analyze the most common defects and their causes.

**Objective:** taking into account the above, was to analyze the data of the State Statistics Service on maternal and infant mortality during pregnancy, childbirth and the postpartum period and compare it with the analysis of «Expert Conclusions» in cases of evaluation of obstetric and gynecological care.

## MATERIALS AND METHODS

The material of the research was the data of the State Statistics Service on maternal and infant mortality during pregnancy, childbirth and the postpartum period (625), court verdicts in criminal cases under Articles 139 and 140 of the Criminal Code of Ukraine according to the Unified State Register of Judgments of Ukraine (USRJU) from 2009 to 2019, as well as 255 commission forensic medical examinations on «medical cases» for 2013-2019 («Expert conclusions»), performed in the «Main Bureau of Forensic Medical Examination of the Ministry of Health of Ukraine» (MB), including in cases of previous departmental inspections by commissions HD.

The obtained data were subjected to statistical processing by standard methods of descriptive statistics.

## RESEARCH RESULTS AND THEIR DISCUSSION

According to the State Statistics Service, mortality during pregnancy, childbirth and the postpartum period (062 Class XV) tends to decrease from 69 in 2014 to 39 in 2018 (excluding the temporarily occupied territory of the Autonomous Republic of Crimea, Sevastopol and parts of the temporarily occupied territories in Donetsk and Luhansk regions since 2014) [12] (table 1).

During the statistical analysis of the commission forensic medical examinations of the Main Bureau of Forensic Medical Examination of the Ministry of Health of Ukraine regarding the obstetrics and gynecology profile for 2013-2019, conducted personally, it was found that forensic medical examinations for medical care occupy 27.2% in the general structure of all commission examinations – (table 2).

Forensic medical examinations for the provision of obstetric and gynecological medical care occupy a leading place in the overall structure of commission examinations for «medical cases» – 23.1% (255 cases).

A detailed analysis of such examinations revealed that the average age of examined women was 31 years of age, ie of working age and childbearing age.

In these 255 examinations, defects in the provision of medical care were found by expert commissions in 186 cases, which amounted to 72.9%. And of these «defective cases» 62.9% (117 cases) of them were in direct causal connection with an adverse outcome; 35.5% (6 cases) – some defects that were not causally related to the onset of fetal death. In 3 cases of gynecological examinations, there were discrepancies in the records in the medical records, which did not allow to assess the quality of medical care and the connection with the consequences.

83.9% (214 cases) were obstetric, and almost half of them, 47.7% (102 cases), had defects in the provision of medical care that were directly causally related to the adverse outcome. Of these, the commissions of experts identified the following defects in the provision of medical care: 46.1% (47) of examinations, the defects in the provision of medical care were directly causally related to the death of the child; in 22.5% (23) – with extirpation of the uterus (severe injuries) and the onset

Table 1

**Distribution of deaths by causes of death during pregnancy, childbirth and the postpartum period for 2013-2018 according to the State Statistics Service**

Causes of death	2013	2014	2015	2016	2017	2018
062 Class XV Pregnancy, childbirth and the postpartum period O00-O99	65	69	60	46	30	39
063 Pregnancy with abortive consequence O00-O08	2	3	3	2	1	1
064 Other direct causes of obstetric death (excluding obstetric tetanus (A34)) O10-O92	35	41	30	32	18	24
065 Other complications of pregnancy, childbirth and the postpartum period O95-O97	1	1	–	–	–	–
066 Indirect causes of obstetric death (excluding human immunodeficiency virus (HIV) disease (B20-B24)) O98-O99	27	24	27	19	11	14

Table 2

**The number of forensic medical examinations according to the State Institution «MB» for 2013-2019**

	2013	2014	2015	2016	2017	2018	2019
The total number of examinations	633	641	663	752	511	446	421
Number of examinations for "medical cases"	149	151	145	147	205	153	157
Number of obstetric and gynecological examinations	25	21	37	46	27	47	52

of fetal death; in 15.7% (16) – with the onset of severe consequences in both women and children (severe injuries in both); in 9.8% (10) – with central nervous system damage in a child (severe injuries); other cases (8): shortcomings during abortion in direct causal connection with the onset of severe consequences (removal of the kidney) – severe injuries and when untimely diagnosis of fetal malformations led to the impossibility of timely termination of pregnancy

15 examinations concerned neonatology, among which in most cases (10) there was a direct causal link between defects in medical care and the death of the child.

Of the defects, in all cases there were incorrectly chosen tactics of childbirth, as well as in most cases – 125 cases out of 186 cases with defects (67.2%) – untimely provision or failure to provide medical care. The reason for the incorrectly chosen tactics of childbirth was under-examination of pregnant women, underestimation of survey data (for example, the case when a physiologically narrow pelvis doctor-obstetrician-gynecologist decided to «let in physiological childbirth», which resulted in death and serious injuries to the mother). In all these cases, doctors had a real opportunity to prevent serious consequences, as 98 cases occurred in large cities of Ukraine (the hospitals had all the necessary equipment and specialists).

When assessing the provision of medical care at different stages, it was found that at the pre-hospital stage (in the clinic) defects were allowed in 45 cases (24.2%), and at the hospital – in 141 cases (75.8%), in particular, during resuscitation measures.

When analyzing 255 of these examinations for obstetrics and gynecology, it was found that in the vast majority of cases – 223 (87.5%) of all examinations for obstetrics received by the MB, contained the conclusions of departmental commissions of the HD.

Upon closer examination of such examinations and comparison of results, it was found that only in 51 cases (22.8%) there was a complete coincidence of the conclusions of the commissions of the Bureau of Forensic Medicine and the HD, and only in cases of significant defects that were in direct causal connection with the consequences. In other cases, the departmental commissions of the HD did not find defects in the provision of medical care, when, according to the results of forensic examinations, the defects were still present and led to serious consequences for women and / or children (death, serious injuries). It should be noted that the analysis of the conclusions of the HD commissions found that in almost all cases the commissions included doctors who were in one way or another connected with the accused medical workers (for example, were their supervisors or simply worked with them in the same institution).

At the same time, an analysis of 53 court verdicts according to the USRJU revealed that 13 of them were related to obstetrics and gynecology, and 12 of them were convictions [13]. In all cases, the source of evidence in the

cases was exclusively the «Expert Conclusions», which clearly stated the existence of a defect in the provision of medical care, its connection with the consequence and the possibility of preventing this consequence.

It should be noted that in addition to the lack of a single algorithm of expert actions, which would be clearly indicated in the relevant document, complicate the forensic assessment of the quality of care such factors as: lack of certain protocols for care (eg, obstetric protocols in thrombosis and embolism during or after childbirth, etc.), which could facilitate forensic assessment of medical care in certain circumstances, poorly completed medical records of the victim, lack of information about the woman's health before pregnancy or the development of pathological conditions, electronic documentation.

## CONCLUSIONS

1. In conducting our own research, it was found that forensic medical examinations for obstetrics and gynecology occupy a leading place in the overall structure of commission examinations for «medical cases», in the vast majority of examinations revealed defects in medical care were in direct causal consequential connection with an adverse consequence. This underscores the low level of obstetric and gynecological care in Ukraine.

2. A small percentage (22.8%) of the coincidence of the results of the commissions of the Bureau of Forensic Medical Examination and the Health Departments in cases of obstetric and gynecological medical care in Ukraine may be due to biased assessment of medical care by the commissions of the Health Departments, which violates the principles of impartiality and legality of assessment.

3. In our opinion, need to develop and implement in practice «Rules of forensic examinations in cases of bringing medical workers to justice for» professional offenses «by the relevant competent institutions (« Main Bureau of Forensic Medicine of the Ministry of Health of Ukraine »), and procedural regulation of the seizure of electronic medical records by law enforcement officials for forensic examination, which will improve the quality of such examinations in Ukraine and increase the level of detection of crimes in the field of medical care.

Конфлікт інтересів: відсутній /

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## REFERENCES

1. Kohn LT, Corrigan JM, Donaldson MS. To Err is Human: Building a Safer Health System // Institute of Medicine (US) Committee on Quality of Health Care in America. Washington (DC): National Academies Press (US). 2000, 1 (1). PMID: 25077248. DOI: <https://www.ncbi.nlm.nih.gov/pubmed/25077248>
2. Kathleen Sutcliffe. The Health Care Industry Needs to Be More Honest About Medical Errors // Time USA. 2019 Nov 05. URL: <https://time.com/5717545/medical-errors/>

3. [In the United States, medical errors have been cited as one of the leading causes of death] // Interfax. 2016. [in Russian]. URL: <http://www.interfax.ru/world/506759>
4. [Medical error: causes and consequences] // Medical and legal portal «103-law.org.ua». 2012. [in Ukrainian]. URL: <http://103-law.org.ua/Article.aspx?a=61>
5. [In Ukraine there are no statistics of medical errors, - the expert] // Analytical online publication of Lviv «Zaxid.net». 2012. [in Ukrainian]. URL: [https://zaxid.net/v\\_ukrayini\\_nema\\_statistiki\\_likarskih\\_pomilok\\_ekspert\\_n1266352](https://zaxid.net/v_ukrayini_nema_statistiki_likarskih_pomilok_ekspert_n1266352)
6. [Medical error and how to deal with it] // Agency of regional information and analytics «galinfo.com.ua». 2013. [in Ukrainian]. URL: [http://galinfo.com.ua/articles/likarska\\_pomylka\\_i\\_yak\\_z\\_neyu\\_borotysya\\_125439.html](http://galinfo.com.ua/articles/likarska_pomylka_i_yak_z_neyu_borotysya_125439.html)
7. Bushmeleva N.N. [Defects in the provision of medical care in cases of maternal death at the regional level] // Electronic scientific journal «Social Aspects of Population Health». 2014. 3 (37). [in Russian]. URL: <http://vestnik.mednet.ru/content/view/565/30/lang,ru/>
8. Mateikovich EA, Shevlyukova TP, Kukarskaya EY, Galieva GD. [Medical errors in the provision of obstetric and gynecological care] // Modern problems of science and education. 2018. 5 (1). [in Russian]. URL: <http://www.science-education.ru/ru/article/view?Id=27991>
9. Steblyuk VV. [Legal and moral and ethical aspects of criminal offenses in the field of professional activity of medical workers] // Forensic examination. 2013. 2: 45-8. [in Ukrainian]. [http://nbuv.gov.ua/UJRN/sme\\_2013\\_2\\_14](http://nbuv.gov.ua/UJRN/sme_2013_2_14)
10. Dunaevskaya LG. [Investigation of crimes committed during the provision of medical care]. Kyiv: UMCC Center; 2012. 168 p. [in Ukrainian]. ISBN 978-966-8287-34-3.
11. Criminal Procedure Code of Ukraine // Information of the Verkhovna Rada of Ukraine (VVR). 2016. [in Ukrainian]. URL: <http://zakon2.rada.gov.ua>
12. Distribution of deaths by sex, age groups and causes of death (0,1) // Database of State Statistics of Ukraine. [in Ukrainian]. URL: <http://database.ukrcensus.gov.ua/Mult/Dialog/Saveshow.asp>
13. Unified State Register of Judgments of Ukraine. 2020. [in Ukrainian]. URL: <http://www.reyestr.court.gov.ua/>

## СУДОВО-МЕДИЧНІ ТА ПРАВОВІ АСПЕКТИ НАДАННЯ МЕДИЧНОЇ ДОПОМОГИ В АКУШЕРСТВІ ТА ГІНЕКОЛОГІЇ

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**Актуальність.** Інколи статистика лікарських помилок замовчується, а інформація про окремі інциденти стає відомою завдяки засобам масової інформації.

**Мета:** встановлення найбільш частих дефектів акушерсько-гінекологічного профілю та їх причин шляхом проведення аналізу даних Державної служби статистики щодо материнської смертності та смертності немовлят під час вагітності, пологів та післяпологового періоду і зіставити його з судово-медичним аналізом надання медичної допомоги акушерсько-гінекологічного профілю.

**Матеріали та методи.** Проаналізовано 625 випадків за даними Державної служби статистики по материнській смертності та смертності немовлят під час вагітності, пологів та післяпологового періоду, судові вирок у кримінальних справах за статтями 139 і 140 Кримінального кодексу України, за даними Єдиного державного реєстру судових рішень України (ЄДРСР) з 2009 р по 2019 р, а також дані з комісійних судово-медичних експертиз за «лікарськими справами» за 2013-2019 рр., виконані в ДУ «Головне бюро судово-медичної експертизи МОЗ України», в тому числі у випадках попередніх відомчих перевірок комісіями Управління охорони здоров'я. Отримані дані піддавалися статистичній обробці стандартними методиками описової.

Результати. У зазначених 255 експертизах дефекти в наданні медичної допомоги були знайдені експертними комісіями в 186 випадках, що склало 72,9%. Причому з цих «дефектних випадків» 62,9% (117 випадки) знаходилися в прямому причинно-наслідковому зв'язку з несприятливим результатом; 35,5% (6 випадків) - деякі недоліки, які не мали причинного зв'язку з настанням смерті плоду. У 3х випадках експертиз по гінекології були протиріччя в записах в медичній документації, що не дозволяло оцінити якість надання медичної допомоги і зв'язок з наслідками. На догоспітальному етапі (в поліклініці) дефекти допускалися в 24,2%, а на госпітальному - в 75,8%. При наявності відомчих перевірок в 23% можна говорити про повний збіг результатів висновків комісії бюро судово-медичної експертизи і УОЗ, причому тільки у випадках суттєвих дефектів в прямому причинному зв'язку з наслідками. У той же час при аналізі 53 судових вироків за даними реєстру судових рішень виявилось, що 13 з них стосуються акушерсько-гінекологічного профілю, причому 12 з них були обвинувальними. У всіх випадках джерелом доказів у справах були виключно «Висновки експерта».

**Висновки.** Було встановлено, що судово-медичні експертизи з надання медичної допомоги акушерсько-гінекологічного профілю займають провідне місце в загальній структурі комісійних експертиз по «лікарських справах», в переважній більшості експертиз виявлені дефекти надання медичної допомоги, що знаходилися в прямого причинно-наслідкового зв'язку з несприятливим результатом.

**Ключові слова:** судово-медична експертиза, акушерство, гінекологія, дефект, надання медичної допомоги.

## СУДЕБНО-МЕДИЦИНСКИЕ И ПРАВОВЫЕ АСПЕКТЫ ОКАЗАНИЯ МЕДИЦИНСКОЙ ПОМОЩИ В АКУШЕРСТВЕ И ГИНЕКОЛОГИИ

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**Актуальность.** Иногда статистика врачебных ошибок замалчивается, а информация об отдельных инцидентах становится известной благодаря средствам массовой информации.

**Цель:** установление наиболее частых дефектов акушерско-гинекологического профиля и их причин путем проведения анализа данных Государственной службы статистики по материнской смертности и смертности младенцев во время беременности, родов и послеродового периода и сопоставить его с судебномедицинским анализом оказания медицинской помощи акушерско-гинекологического профиля.

**Материалы и методы.** Проанализировано 625 случаев, по данным Государственной службы статистики по материнской смертности и смертности младенцев во время беременности, родов и послеродового периода, судебные приговоры по уголовным делам по статьям 139 и 140 Уголовного кодекса Украины, по данным Единого государственного реестра судебных решений Украины (ЕГРСР) с 2009 г. по 2019 г., а также данные из комиссионных судебно-медицинских экспертиз по «лекарственным делам» за 2013-2019 гг., выполненные в ГУ «Главное бюро судебно-медицинской экспертизы МЗ Украины», в том числе и в случаях предыдущих ведомственных проверок комиссиями Управления охраны здоровья. Полученные данные подвергались статистической обработке стандартными методиками описательной статистики.

**Результаты.** В указанных 255 экспертизах дефекты в оказании медицинской помощи были найдены экспертными комиссиями в 186 случаях, что составило 72,9%. Причем из этих «дефектных случаев» 62,9% (117 случаев) находились в прямом причинно-следственной связи с неблагоприятным исходом; 35,5% (6 случаев) - в некоторые недостатки, которые не имели причинной связи с наступлением смерти плода. В 3х случаях экспертиз по гинекологии были противоречия в записях в медицинской документации, не позволяли оценить качество оказания медицинской помощи и связь с последствиями. На догоспитальном этапе (в поликлинике) дефекты допускались в 24,2%, а на госпитальном - в 75,8%. При наличии ведомственных проверок в 23% имело место полное совпадение результатов выводов комиссий бюро судебно-медицинской экспертизы и УОЗ, причем только в случаях существенных дефектов в прямой причинной связи с последствиями. В то же время при анализе 53 судебных приговоров по данным реестра судебных решений оказалось, что 13 из них касаются акушерско-гинекологического профиля, причем 12 из них были обвинительными. Во всех случаях источником доказательств по делам были исключительно «Выводы эксперта».

**Выводы.** Было установлено, что судебно-медицинские экспертизы по оказанию медицинской помощи акушерско-гинекологического профиля занимают ведущее место в общей структуре комиссионных экспертиз по «врачебным делам», в подавляющем большинстве экспертиз обнаружены дефекты оказания медицинской помощи, находившиеся в прямой причинно-следственной связи с неблагоприятным исходом.

**Ключевые слова:** судебно-медицинская экспертиза, акушерство, гинекология, дефект, оказания медицинской помощи.

## DIAGNOSIS OF ALCOHOL INTOXICATION IN VICTIMS OF EMERGENCIES

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**Relevance.** In the case of death from injury, the question of whether the victim was intoxicated and to what extent, as the presence of alcohol intoxication could have affected the thanatogenesis of death is important. A reliable method of determining the concentration of ethanol in the body is its study in the blood, urine, and cerebrospinal fluid. But in extreme conditions, in large-scale disasters, during military conflicts, there may be difficulties in the selection, storage, transportation, and research of biological fluids. Therefore, the search for reliable non-invasive rapid methods is relevant.

**Objective** is the development of a set of criteria for improving the accuracy of detecting the presence of ethanol and determining its amount in deaths due to trauma in emergencies by non-invasive rapid methods.

**Materials and methods.** Review of scientific publications in international electronic scientometric databases PubMed, Embase, and Scopus by keywords. Search depth - 10 years (2008-2018). Comparison of literature data with the results of own research on the possibility of diagnosing alcohol intoxication to detect the presence and determination of ethanol in biological fluids (saliva, blood, urine) of persons who died and died in emergencies by indicative and evidentiary methods.

**Results.** The possibility of using the non-invasive express method (indicator test strips) as a guide to detecting the presence and quantification of ethanol in the saliva of deaths and deaths from injuries in emergencies, conflicts, in the absence of the necessary conditions for blood storage and urine (lack of power supply, the impossibility of freezing objects, storage, destruction of objects during transportation, etc.) was described. It is proved that the average result of the quantitative content of ethanol in blood and urine, found in the evidence-based method of research (gas-liquid chromatography), coincides and confirms the result obtained by us in conducting a non-invasive rapid method using indicator test strips. In the course of the conducted researches, the conformity concerning objectivity and correctness of detection of the presence and quantitative content of ethyl alcohol with the use of indicator test strips which is confirmed by researches of blood, urine by evidential methods (gas-liquid chromatography) is proved.

**Conclusion.** A non-invasive rapid method (indicator test strips) can be used as a guide to detect the presence of ethyl alcohol and determine its quantitative content in the saliva of the dead and deceased, with subsequent confirmation by evidence-based methods of research (gas-liquid chromatography) of blood, urine.

**Keywords:** diagnosis, alcohol intoxication, ethyl alcohol, test strips, gas-liquid chromatography, dynamics, trauma, mortality.

**Relevance.** Recently, special attention has been paid to the study of traumatic changes that occur in the human body due to the constant increase in the number of man-made disasters, military conflicts, emergencies, industrial and domestic injuries, traffic accidents. The number of deaths and injuries continues to increase every day, so the nature, mechanism, duration of injuries, the presence and impact of alcohol intoxication, development of measures to reduce injuries, provide timely medical care, improve diagnosis, treatment, and prevention of injuries is relevant [1]. It should be noted that in cases of death from injuries, for law enforcement agencies and insurance companies it is often important to ask whether the victim was intoxicated and to what extent, as the presence of alcohol intoxication could affect the thanatogenesis of death, etc. [3-7]. In the literature, much attention has always been paid to the effects of alcohol on the body, especially in injuries. It is proved that a reliable method for determining the concentration of ethyl alcohol in

the body is its study in blood, urine, and cerebrospinal fluid. But quite often in emergency conditions, at large-scale catastrophes, during military conflicts there are difficulties at selection, storage, transportation, and research of biological liquids. These difficulties arise due to limited technical equipment of laboratories, lack of power supply, the impossibility of freezing objects, destruction during transportation [2]. In the injured, indicative methods can be used to detect the presence of alcohol intoxication and its degree: breathalyzers to determine the alcohol content in the exhaled air; indicator test strips for measuring the content of ethyl alcohol in human saliva and urine, etc., with which you can perform a rapid analysis.

The objective of this work was to develop a set of criteria to improve the accuracy of detecting the presence of ethyl alcohol and determine its quantitative content in the dead and deceased due to trauma in emergencies by non-invasive rapid methods.

## MATERIAL AND METHODS

The material of the study was biological fluids (saliva, blood, urine) of 32 of males and females, aged 20 to 60 years, who died from injuries and were dissected in the thanatopsy department of the Bureau of Forensic Medicine of Luhansk region. To determine the amount of ethyl alcohol were used: indicator test strips (in the study of saliva), the method of gas-liquid chromatography (in the study of blood and urine), followed by statistical analysis of the results. The anamnestic data, data on the mechanism of an injury, and circumstances of its reception were considered, in the present medical documentation, results of laboratory researches were studied, and also results of section research of a corpse were considered.

The method using indicator strips has a high sensitivity to the primary alcohols in the biological fluid, namely: ethanol, propanol, methanol. The method with the detection of ethanol content in the saliva is based on a highly specific enzymatic reaction of oxidation of primary alcohols to aldehyde and hydrogen peroxide. Due to the action of hydrogen peroxide in the presence of the enzyme peroxidase, the chromogen is oxidized, resulting in the formation of a colored compound. The degree of color is proportional to the alcohol content in saliva.

To determine the alcohol in the saliva of the deceased, a test strip was inserted into the oral cavity of the deceased so that the sensory part of the strip was completely immersed in saliva; after 10 s (using a stopwatch), the strip was removed from the oral cavity and cleaned of excess saliva on the sensory part. Then the strip was placed on a clean dry and flat surface so that the touch part was on top. After two minutes, evaluated the degree of the color of the sensor element and determine the concentration of ethanol on the color scale, which is on the package with insufficient light.

For the semi-quantitative determination of ethanol in saliva, the color of the indicator part was compared with the corresponding color field of the color scale. There are five color areas that correspond to the following ethanol concentration: yellow - 0.0%; light green - 0.02% (or 0.2 ‰); lime - 0.05% (0.5 ‰); green - 0.1% (1 ‰); dark green - 0.2% (2 ‰).

If the color changed only the outer boundaries of the sensor part, and the color of the Central part did not change, the test was repeated.

To confirm the reliability of the result, studies were performed to detect and quantify ethanol in blood and urine according to the generally accepted method on a gas chromatograph «Chromatek-Crystal 5000.2». To do this, after conversion of ethanol and other aliphatic alcohols into lighter compounds - alkyl nitrites - by reacting alcohols with sodium nitrite and trichloroacetic (THO) acid, which are separated, depending on the polarity and boiling point, on a chromatographic column filled with solid support with the applied liquid phase at a certain constant temperature, and eluted with an inert carrier gas at a certain flow rate into the detector, the signal of which is amplified and recorded in the form of

a chromatogram with peaks. Each peak corresponds to the absolute retention time of a particular component, which is pre-determined when setting the calibration characteristics. The calculation of the amount of ethanol is performed by the method of internal standard, which uses isopropanol or n-propanol. In this case, the areas or heights of the ethyl nitrite peaks and the internal standard are measured automatically, and using the coefficients previously calculated during the calibration by the method of least squares, the concentration of ethyl alcohol in the biological fluid (blood, urine) is calculated. The heights or areas of the peaks are measured in units of the response of the detector, in this case - millivolts for the height of the peak, and the ratio of height to width at half height - for the area of the peak.

The work was carried out in accordance with the requirements of the «Instruction on forensic examination» (order of the Ministry of Health of Ukraine № 6 from 17.01.1995), in accordance with the requirements and norms, standard regulations on ethics of the Ministry of Health of Ukraine № 690 from 23.09.2009, «The procedure for removing biological objects from the dead, the bodies of which are subject to forensic examination and pathological examination, for scientific purposes (2018)».

## RESULTS AND DISCUSSION

Compliance with the objectivity and correctness of detection of the presence and quantitative content of ethyl alcohol using the semi-quantitative method (indicator test strips) is confirmed by blood and urine tests by evidence-based methods (gas-liquid chromatography).

Let's show it by example. M.'s husband, 36, died. When examining saliva with an indicator test strip, the color of the strip changed to a greenish color, which corresponded to an ethanol concentration of 0.1%, or 1 ‰, (Fig. 1, A), which indicates a slight degree of alcohol intoxication. When using the evidence-based method (gas-liquid chromatography), the average result of the quantitative content of ethanol in the blood was 0.95% (average value with a deviation of not more than 5%) (Fig. 1, B). At the research of urine gr. M. by gas-liquid chromatography revealed an average result of ethanol content in urine of 1.48% (average value with a deviation of not more than 5%) (Fig. 1, B).

Thus, the detected average result of the quantitative content of ethanol in the blood was 0.95% in a patient M, was detected in the evidence-based method of research (gas-liquid chromatography) the content of ethyl alcohol confirms the result obtained by us when conducting a non-invasive rapid method using indicator test strips, which revealed the presence of alcohol and quantitative content corresponding to mild alcohol intoxication.

The average result of the quantitative content of ethanol, which in urine is 1.48 ‰ was detected by the evidence-based method of research (gas-liquid chromatography), and the content of ethyl alcohol was detected by the method of gas-liquid chromatography

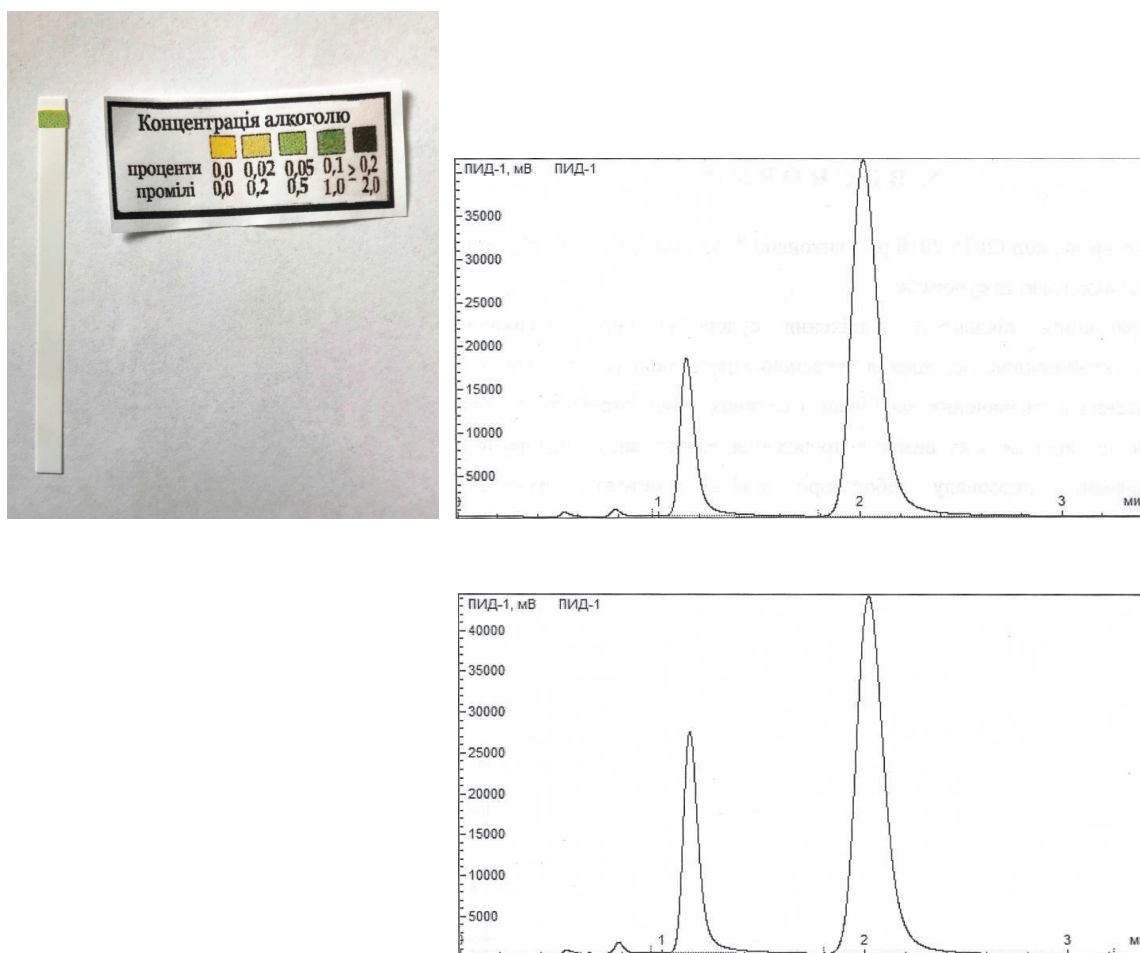


Fig. 1. The content of ethanol in different biological fluids in casualty M., determined in different ways:  
 A. In saliva, according to the indicator test strip – 0,1 %.  
 Б. In the blood, according to gas-liquid chromatography – 0,95 %.  
 В. In urine, according to gas-liquid chromatography – 1,48 %.

in the blood - 0.95 % in a patient M; as well as when conducting a non-invasive rapid method using indicator test strips, was detected the presence of alcohol and quantitative content, which corresponded to a mild degree of alcohol intoxication, in which the concentration of alcohol is from 0.5 ‰ to 1.49 ‰.

The obtained research results show that our data coincide with the literature on the possibility of detecting and quantifying the method of ethyl alcohol in saliva by an indicative method using indicator test strips and evidence-based methods for living persons as a rapid diagnosis to determine the presence and degree of alcoholism as well as in persons with traumatic injuries, but it should be noted that we have for the first time demonstrated the possibility of using non-invasive methods in the study of the saliva of the dead [1, 2].

**CONCLUSION**

Demonstrated the possibility of using non-invasive rapid methods (indicator test strips to detect the presence of

ethyl alcohol and determine its quantitative content in the saliva of casualty and deaths from injuries in emergencies, conflicts in the absence of necessary conditions for blood and urine storage) freezing of objects, storage, destruction of objects during transportation, etc.). Correspondence with the objectivity and correctness of detection of the presence and quantitative content of ethyl alcohol using indicator test strips confirmed by blood and urine tests (gas-liquid chromatography). It is shown that the average result of the quantitative content of ethanol in the blood, found in the evidence-based method of research (gas-liquid chromatography) coincides and confirms the result obtained by a non-invasive rapid method using indicator test strips, which revealed the presence of alcohol and content, which corresponded to a mild degree of alcohol intoxication in the dead and deceased in the presence of traumatic injuries.

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## REFERENCES

1. Dubrov S.A. [Basic principles of intensive care of patients with early polytrauma. Optimization Methods] // Medical Sciences. 2015; 5 (4): 117-23. [in Russian] doi: 10.15587/2313-8416.2015.43309
2. Pavlov AL, Savin AA, Bogomolov DV, Pavlova AZ, Larev ZV. [Clinical pathomorphology and thanatogenesis of various forms of alcohol intoxication] // Sud Med Expert. 2018; 3: 11-4. [in Russian]. doi: 0.17116/sudmed201861311-14
3. Vonghia L, Leggio L, Ferrulli A, Bertini M, Gasbarrini G, Addolorato G. Alcoholism Treatment Study Group. Acute alcohol intoxication // Eur J Intern Med. 2008; 19 (8): 561-7. doi: 10.1016/j.ejim.2007.06.033
4. Bond J, Witbrodt J, Ye Y, Cherpitel CJ, Room R, Monteiro MG. Exploring structural relationships between blood alcohol concentration and signs and clinical assessment of intoxication in alcohol-involved injury cases // Alcohol Alcohol. 2014; 49 (4): 417-22. doi: 10.1093/alcalc/agu014
5. McCartney D, Desbrow B, Irwin C. Using alcohol intoxication goggles (Fatal Vision® goggles) to detect alcohol related impairment in simulated driving // Traffic Inj Prev. 2017; 18 (1): 19-27. doi: 10.1080/15389588.2016.1190015
6. Foster CA, Dissanaik ShD. Prevalence and consequences of positive blood alcohol levels among patients injured at work. Prevalence and consequences of positive blood alcohol levels among patients injured at work // J Emerg Trauma Shock. 2014; 7 (4): 268-73. doi: 10.4103/0974-2700.142748
7. Cash C, Peacock A, Barrington H, Sinnett N, Bruno R. Detecting impairment: sensitive cognitive measures of dose-related acute alcohol intoxication // J Psychopharmacol. 2015; 29 (4): 436-46. doi: 10.1177/0269881115570080

## ДІАГНОСТИКА АЛКОГОЛЬНОГО СП'ЯНІННЯ У ЗАГИБЛИХ ПРИ НАДЗВИЧАЙНИХ СИТУАЦІЯХ

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**Актуальність.** У випадках смерті від травм важливе значення має питання, чи знаходився загиблий в стані алкогольного сп'яніння і якого ступеню, як наявність алкогольного сп'яніння могла вплинути на танатогенез смерті. Достовірним методом визначення концентрації етанолу в організмі є його дослідження в крові, сечі та лікворі. Але в надзвичайних умовах, при масштабних катастрофах, під час військових конфліктів можуть виникати труднощі при відборі, збереженні, транспортуванні і дослідженні біологічних рідин. Тому актуальним є пошук надійних неінвазивних експрес-методів.

**Мета.** Розробка комплексу критеріїв підвищення точності виявлення наявності етанолу та визначення його кількості у померлих внаслідок травми в умовах надзвичайних станів неінвазивними експрес-методами.

**Матеріали та методи.** Огляд наукових публікацій в міжнародних електронних наукометричних базах даних PubMed, Embase і Scopus за ключовими словами. Глибина пошуку – 10 років (2008-2018 рр). Співставлення літературних даних з результатами власних досліджень, про можливість діагностики алкогольного сп'яніння по виявленню наявності і визначенню кількості етанолу в біологічних рідинах (слина, кров, сеча) осіб, померлих та загиблих в умовах надзвичайних ситуацій, орієнтовними і доказовими методами.

**Результати.** Продемонстрована і наведена можливість використання неінвазивного експрес-методу (індикаторних тест-смужок), як орієнтовного, для виявлення факту наявності та визначення кількісного вмісту етанолу в слині померлих та загиблих від травм в умовах надзвичайних станів, конфліктів, при відсутності необхідних умов для зберігання крові і сечі (відсутність електропостачання, неможливість заморозки об'єктів, зберігання, руйнування об'єктів під час транспортування, тощо). Доведено, що середній результат кількісного вмісту етанолу в крові і сечі, виявлений при проведенні доказового методу дослідження (газо-рідинної хроматографії), співпадає і підтверджує результат, отриманий нами при проведенні неінвазивного експрес-методу з використання індикаторних тест-смужок. В ході проведених досліджень доведена відповідність щодо об'єктивності і правильності виявлення наявності і кількісного вмісту етилового спирту з використанням індикаторних тест-смужок, яка підтверджена дослідженнями крові, сечі доказовими методами (газо-рідинної хроматографії).

**Висновок.** Неінвазивний експрес-метод (індикаторні тест-смужки) може бути використаний, як орієнтовний, для виявлення факту наявності етилового спирту та визначення його кількісного вмісту в слині померлих і загиблих, з подальшим підтвердженням доказовими методами дослідження (газо-рідинної хроматографії) крові, сечі.

**Ключові слова:** діагностика, алкогольна інтоксикація, етиловий спирт, тест-смужки, газо-рідинна хроматографія, динаміка, травма, смертність.

## ДИАГНОСТИКА АЛКОГОЛЬНОГО ОПЬЯНЕНИЯ У ПОГИБШИХ ПРИ ЧРЕЗВЫЧАЙНЫХ СИТУАЦИЯХ

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**Актуальность.** В случаях смерти от травм важное значение имеет вопрос, находился ли погибший в состоянии алкогольного опьянения и какой степени, как наличие алкогольного опьянения могло повлиять на танатогенез смерти. Достоверным методом определения концентрации этанола в организме является его исследования в крови, моче и ликворе. Но в чрезвычайных условиях, при масштабных катастрофах, во время военных конфликтов могут возникать трудности при отборе, хранении, транспортировке и исследовании биологических жидкостей. Поэтому актуальным является поиск надежных неинвазивных экспресс-методов.

**Цель.** Разработка комплекса критериев повышения точности выявления наличия этанола и определения его количества у умерших вследствие травмы в условиях чрезвычайных ситуаций неинвазивными экспресс-методами.

**Материалы и методы.** Обзор научных публикаций в международных электронных наукометрических базах данных PubMed, Embase и Scopus по ключевым словам. Глубина поиска - 10 лет (2008-2018 гг). Сопоставление литературных данных с результатами собственных исследований, о возможности диагностики алкогольного опьянения по выявлению наличия и определению количества этанола в биологических жидкостях (слюна, кровь, моча) лиц, умерших и погибших в условиях чрезвычайных ситуаций, ориентировочными и доказательными методами.

**Результаты.** Продемонстрирована и приведена возможность использования неинвазивного экспресс-метода (индикаторных тест-полосок), как ориентировочного, для выявления факта наличия и определения количественного содержания этанола в слюне умерших и погибших от травм в условиях чрезвычайных положений, конфликтов, при отсутствии необходимых условий для хранения крови и мочи (отсутствие электроснабжения, невозможность заморозки объектов, хранения, разрушения объектов во время транспортировки и т.д.). Доказано, что средний результат количественного содержания этанола в крови и моче, обнаруженный при проведении доказательного метода исследования (газо-жидкостной хроматографии), совпадает и подтверждает результат, полученный нами при проведении неинвазивного экспресс-метода при использовании индикаторных тест-полосок. В ходе проведенных исследований доказано соответствие объективности и правильности выявления наличия и количественного содержания этилового спирта с использованием индикаторных тест-полосок, подтвержденное исследованиями крови, мочи доказательными методами (газо-жидкостной хроматографии).

**Вывод.** Неинвазивный экспресс-метод (индикаторные тест-полоски) может быть использован, как ориентировочный, для выявления факта наличия этилового спирта и определения его количественного содержания в слюне умерших и погибших, с последующим подтверждением доказательными методами исследования (газо-жидкостной хроматографии) крови, мочи.

**Ключевые слова:** диагностика, алкогольная интоксикация, этиловый спирт, тест-полоски, газо-жидкостная хроматография, динамика, травма, смертность.

## INDOMETHACIN & SARS-COV-2: PROSPECTS FOR CLINICAL MANAGEMENT OF THE INFLAMMATORY STATE. Review

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**Actuality.** Severe acute respiratory syndrome- (SARS) is a pandemic (called as SARS-CoV-2 or COVID-19), severely affected by transmission and fatal disease caused by unknown coronavirus family of RNA virus (SARS-COV). Phenotype can range from asymptomatic to fulminate cytokine storm which leads multiorgan failure resulting death. Still the world is eagerly waiting for antiviral drug to stop the corona virus infection. Previous studies found that indomethacin had ability to inhibit the RNA and DNA virus replication.

**Objectives.** Discuss the possibility of clinical treatment of inflammation caused by SARS-COV-2 with indomethacin.

**Materials and methods.** Analysis of scientific publications in the international electronic scientometric database PubMed by keywords for the period 1991-2020. Comparison with clinical cases.

**Results.** Interleukins, Interferons and metabolites formed by the enzyme cyclooxygenase (COX 1/COX 2) are active against some RNA viruses. Experts have divided the SARS infection in three phases (phase-1, 2, 3) based on severity of infection. In phase-3 there was "cytokine storm" due to exuberant inflammation observed which can damage organs and even fatal. We investigated that effect of indomethacin on COX inhibitor on coronavirus replication and cytokine storm in reducing the hyper inflammatory state. Indomethacin is a potent inhibitor of SARS CoV-2.

**Conclusion.** Indomethacin can be considered safe and effective for prevention and treatment of coronavirus infection also antiviral activity.

**Key words:** Indomethacin, covid-19, SARS-COV 2, inflammation

**Actuality.** Severe acute respiratory syndrome- (SARS) is a pandemic (called as SARS-CoV-2 or COVID-19), severely affected by transmission and fatal disease caused by unknown coronavirus family of RNA virus (SARS-COV). Phenotype can range from asymptomatic to fulminate cytokine storm which leads multiorgan failure resulting death. Still the world is eagerly waiting for antiviral drug to stop the corona virus infection. Previous studies found that indomethacin had ability to inhibit the RNA and DNA virus replication.

**Objectives.** Discuss the possibility of clinical treatment of inflammation caused by SARS-COV-2 with indomethacin.

**Materials and methods.** Analysis of scientific publications in the international electronic scientometric database PubMed by keywords for the period 1991-2020. Comparison with clinical cases.

**Results.** The global pandemic SARS-COV-2 started from Wuhan, CHINA which has shaken terribly the world. This virus pandemic challenged all healthcare professionals from treating infected people to prevention of infection. This corona virus rapidly infected people in china and spread all over the world. WHO declared this as pandemic disease. This coronavirus has been reported

all the world and 11 419 529 cases with 533 780 deaths have confirmed with 4.674 death rate and continuing. Common symptoms of coronavirus infection were cough, fever, head ache and sputum production. While complicated symptoms are acute respiratory distress syndrome and cardiac injuries [1]. Experts believed that SARS-COV-2 may be transmitted from bats to humans [2]. The main host cell receptor for SARS-COV-2 is ACE2 receptor (angiotensin-converting enzyme 2), this is the main gate for entry of coronavirus and cause infection [3,4] and pathogenesis reveals that all exposed people are infected and not all infected people develops serious problems, but completely depends on the immunity of specific person. The experts divided the infection into three phases, phase-1 asymptomatic incubation period may be or may not be with detectable virus, phase-2 symptomatic with presence of virus and need of hospital, phase-3 severe respiratory symptomatic phase with viral load and inflammation due to cytokine burst, considered as dangerous phase.

Phases of SARS-CoV-2 infection. Experts described that infection can be divided into three phases depending on severity; each phase specific therapeutic treatment may be indicated or avoided. Again this specific treatment

can be specific from person to person due to immune variation and also response of patients.

Phase 1 (asymptomatic incubation). In this phase, person has contracted SARS-CoV-2, the infection starts and the immune system responds against the virus. Initial symptoms can be cough, fatigue, fever, nausea and diarrhea. Duration of this phase can be from 3-7 days. During this phase-1, a specific adaptive immune response will be required to break down the virus replication to avoid the progress of disease to severe. Immune responses and development could be certainly most important at this phase. When patient is at this stage antiviral can be helpful to inhibit the viral load and avoid further complications with the prevention of virus replication. Most probably only antiviral could be more effective to stimulate the immune system and avoiding the use of steroid or non-steroid anti-inflammatory drugs, and being able to take into consideration the administration of immune stimulants or plasma derived from cured patients by convalescent plasma could be beneficial.

Currently, there is evidence of antiviral drugs remdesivir, lopinavir/ritonavir, chloroquine and hydroxychloroquine for efficiency against SARS-CoV-2. If the progress of infection is limited in this phase and if virus is defeated, this will be a very good chance for the recovery without further complications.

Phase 2 (symptomatic). The second phase of infection begins between the 10th and 14th day. A protective immune response of the body is impaired; the immune system was not able to protect body from the virus and deep respiratory tract infection, as the lungs.

The hypoxic phase starts; in this phase hospitalization and oxygen administration can be required. Cardiac involvement and clotting problems could take place in this phase and patients with underlying heart disease could have a greater risk of entering the serious clinical picture. Laboratory tests show a decrease in lymphocytes, an increase in transaminases and a moderate increase in pro-inflammatory markers.

The treatment that could be indicated is a continuous use of anti-viral drugs and, when the respiratory situation worsens, need to be started the support of oxygen and/or use of anti-inflammatory drugs, antibiotics and the administration of LMWH-(Low-molecular-weight-heparin) to prevent thromboembolic events.

Phase 3 (severe). The third stage is the most serious, which can lead to the death of the patient. In this phase there is a hyperactive and systemic (not only lung) inflammatory state which is called Cytokine Storm (CS) and that can appear in the patient and, briefly, lead to respiratory distress syndrome (ARDS). In this phase inflammation marker values (IL-2, IL-6, GCSF, TNF-alpha, D-dimer, ferritin, etc.) are very high. The patient may have severe respiratory failure and cardiac shock. All the organs of different systems may see a worsened condition. Immunological therapies (corticosteroids, anti-

interleukin 6, such as tocilizumab and sarilumab, IL-1 receptor antagonists such as anakinra or canakinumab, JAK-inhibitors, convalescent plasma transfusion) are necessities at this severe stage to attempt the reduction of an aberrant storm cytokinetic response. The prognosis for patients at this stage of disease is very severe [5-9].

Indomethacin. Indomethacin is an inexpensive drug, non-selective cyclooxygenase (COX) inhibitor that can inhibit COX-1 and COX-2 which catalyses the production of prostaglandins, and also used to treat a variety of inflammatory conditions. Indomethacin is a potent anti-inflammatory agent, anti-viral and inhibits COX enzymes more potently than aspirin [10] with other mechanisms like inhibiting movement of PML (Polymorpho nuclear leucocytes), multidrug resistance protein. Amici et al. confirmed indomethacin possesses antiviral activity in vitro against SARS CoV (severe acute respiratory syndrome coronavirus) in monkey VERO cells as well as in vivo activity at relatively low doses (1 mg/kg) against canine coronavirus (C CoV) in dogs and also indomethacin possesses direct antiviral activity for SARS CoV and C CoV by blocking viral RNA synthesis many folds. Indomethacin is a NSAID which was introduced in the 1965 by FDA and has been used broadly for the treatment of pain and inflammatory conditions. There is a rational basis for the use of indomethacin in the treatment of Covid-19, in preference to other NSAIDs [11].

United States have been using indomethacin in the treating the COVID-19 symptoms for some time and now have experienced of using the indomethacin in more than 60 patients. Among Dr Jonathan Leibowitz, Dr Robert Rothstein and Dr Aline Benjamin, have shared their insights and experiences while treating the patients of COVID-19 [12].

Indomethacin, however, can also induce other side effects such as gastritis, renal dysfunction and platelet dysfunction, [13] which could be detrimental to COVID-19 patients with severe SARS-CoV-2 infection, especially if patients have multiorgan dysfunction/ failure resulting from cytokine storm (C.S). Furthermore, some authors have reported that NSAIDs such as ibuprofen may be detrimental in patients with SARS-CoV-2, causing more severe infection or leads to later complications such as emphysema, prolonged hospital stay, or lung cavitations, as has been reported in patients with bacterial pneumonia [14, 15]. However, the WHO recently did not recommend against ibuprofen use for infection with SARS-CoV-2 [16]. Some studies have shown ibuprofen to cause decrease in sputum IL-6 in cystic fibrosis patients [17] and synovial fluid IL-6 in patients with knee osteoarthritis [17], which demonstrates that NSAIDs can lower IL-6 in human fluids. This lends biologic plausibility that COX inhibition with indomethacin could lower IL-6 levels in nasopharyngeal-respiratory tract secretions. Whether using lower doses of indomethacin (estarting with 25 mg 3 times daily) at first sign of infection (in outpatients

after a positive nasopharynx swab confirmation) or for IPD with adequate organ function and no evidence of cytokine storm is conjectural, but use of this agent along with gastric protective agents (e.g., H2 blockers) may be prudent. Since cytokine storm is result of basically an inflammatory response, well-timed blunting of this cascade with indomethacin could conceivably lower inflammatory mediators such as TNF and IL-6 as well as superoxide free radicals, which invoke the cellular damage [13]. Perhaps a clinical strategy would be to monitor IL-6 levels (or C-reactive protein [CRP] as a surrogate marker), upon admission in noncritical patients and start indomethacin when IL-6 (or CRP) begins to rise, and subsequently monitor levels daily. Indeed, well-timed anti-inflammatory agents such as NSAIDs and corticosteroids have been suggested to reduce systemic inflammation prior to the development of overwhelming systemic inflammation/cytokine storm [18]. Indomethacin could be used alone or more likely, as an adjunct to antiviral therapy such as remdisivir, in noncritical patients. It would be interesting to monitor time to clearance of the antigen from upper respiratory secretion, antibody kinetics, and duration of symptomatic disease in patients treated with indomethacin. Given the cost and availability of this agent, indomethacin may warrant study in outpatients or admitted patients with documented infection with SARS-CoV-2 without evidence of cytokine storm.

**Mechanism of action of Indomethacin.** Indomethacin (INDO) is an NSAID and functions like most other NSAIDs. The effect of indomethacin is due to inhibition the synthesis of prostaglandins. Prostaglandins are produced primarily by the cyclooxygenase (COX) enzymes, and these prostaglandins are very critical mediators of inflammation, fever and pain, also involved in maintaining different system function (renal function, GI mucosa, and platelet activity-inhibition of this enzyme) by NSAIDs. COX-1 has involvement in the production of thromboxane A2 (a critical mediator of platelet aggregation) – thus, inhibition of this enzyme is likely responsible for the anti-platelet effects of NSAIDs. COX-1 appears for maintenance of GI mucosa, while COX-2 seems to be upregulated in inflamed tissues, and responsible for the production of prostaglandins which cause inflammation, fever and pain. Although COX-2 selective NSAIDs may have fewer GI associated side effects, indomethacin is a non-selective COX inhibitor [19].

The NSAID Indomethacin has a potent antiviral activity against different coronaviruses, being effective against the canine (CCoV) and the human (SARS-CoV) coronaviruses [20]. Moreover, INDO does not affect directly virus infectivity, binding to ACE-2 receptor or entry into target cells through respiratory system, but acts very early on the coronavirus replication cycle, selectively blocking viral RNA synthesis. INDO has been used for a long time as a potent anti-inflammatory drug, acting by blocking COX-1 and COX-2 activity and inhibiting

pro-inflammatory prostaglandin synthesis [21]. The antiviral effect, however, appears to be cyclooxygenase-independent, since it occurs at concentrations higher than those needed for COX inhibition (10<sup>-8</sup>,10<sup>-9</sup>M) [22]; in addition, the antiviral activity cannot be mimicked by the potent COX inhibitor Aspirin, which has no effect on either CCoV or SARS-CoV replication up to millimolar concentrations. Indomethacin has anti-viral activity; it down-regulates viral replication, and literature showed its anti-viral activity against rhabdovirus vesicular stomatitis virus, hepatitis B virus and coronavirus [22, 23]. Indomethacin (and most other NSAIDs) can impact most organ systems of the body (gastrointestinal, neurological, renal, hematologic and cardiopulmonary systems). As previously mentioned indomethacin is a non-selective COX inhibitor, and COX-1 is responsible for the production of prostaglandins involved in the maintenance of the gastric mucosa. Inhibition of this process can result in dyspepsia (indigestion), nausea, constipation, and diarrhea [24].

Although no randomized trial data was available for indomethacin for treatment or slowing progression of SARS-CoV-2 infection, these agents should be considered by the medical community as potentially worthy of further study as therapeutic adjuncts, given the relative safety, accessibility, and cost effective. As SARS-CoV-2 infection can be divided into three phases: phase 1, an asymptomatic or slightly symptomatic incubation period with or without detectable virus; phase 2, slightly symptomatic period with presence of virus; phase 3, severely symptomatic respiratory phase with high viral load and generalized hyperinflammatory state. The third is the most severe and dangerous described by a generalized hyperinflammatory state, a sudden release of cytokines into the circulation defined as «cytokine storm» (CS). Waiting to find antivirals directed against SARS-CoV-2, evidence has shown that reducing or stopping the hyperinflammatory state that occurs in some infected patients is effective in improving health. We believe that it is of utmost importance to properly manage the inflammatory/immune status of the infected patient. The use of indomethacin, as well as its proven efficacy in the prophylaxis and treatment of autoinflammatory diseases such as FMF or pericarditis, could be considered in all three stages of SARS-CoV-2 infection, especially in those patients at high risk of developing serious lung complications in a dramatically short time, in monotherapy or in combination, carefully monitoring possible drug interactions. Indomethacin, if used in the recommended doses, could be in monotherapy or in combination a safe and effective treatment for the prevention or reduction of cytokine storm in sars-CoV2. However, we believe that a combination of several drugs, each at a lower dosage than monotherapy, may be the most effective and tolerable solution to manage the patient's inflammatory state, particularly in phases two and three.

## CONCLUSION

Indomethacin can be considered safe and effective for prevention and treatment of coronavirus infection also antiviral activity.

Конфлікт інтересів: відсутній /

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## REFERENCES

- Huang C., Wang Y., Li X., et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020 January 24; 395 (10223):497-506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
- Zhou P., Yang X.-L., Wang X.-G., et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020 Feb 03; 579: 270-273. <https://doi.org/10.1038/s41586-020-2012-7>
- Xu H., Zhong L., Deng J., Peng J., Dan H., Zeng X., Li T. & Chen Q. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci*. 2020 Feb 24; 12: article 8. <https://doi.org/10.1038/s41368-020-0074-x>
- Cao Y., Li L., Feng Z., Wan Sh., P. Huang, Sun X., Wen F., Huang X., Ning G. & Wang W. Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations. *Cell Discovery*. 2020 Feb 24; 6(1): article 11. <https://doi.org/10.1038/s41421-020-0147-1>
- Shi Y., Wang Y., Shao Ch., Huang J., Gan J., Huang X., Bucci E., Piacentini M., Ippolito G., Melino G. COVID-19 infection: the perspectives on immune responses. *Cell Death & Differentiation*. 2020 March 23. 27: 1451-4. <https://doi.org/10.1038/s41418-020-0530-3>
- Goodman R.B., Strieter R.M., Martin D.P., Steinberg K.P., Milberg J.A., Maunder R.J., Kunkel S.L., Walz A., Hudson L.D., Martin T.R. Inflammatory cytokines in patients with persistence of the acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 1996;154:602-11. PMID: 8810593. <https://doi.org/10.1164/ajrccm.154.3.8810593>
- Arend W.P. Interleukin-1 receptor antagonist. *Adv Immunol*. 1993; 54: 167-227. PMID: 8379462. [https://doi.org/10.1016/s0065-2776\(08\)60535-0](https://doi.org/10.1016/s0065-2776(08)60535-0)
- Burger D., Chicheportiche R., Giri J.G., Dayer J.M. The inhibitory activity of human interleukin-1 receptor antagonist is enhanced by type II interleukin-1 soluble receptor and hindered by type I interleukin-1 soluble receptor. *J Clin Invest*. 1995 July 1; 96: 38-41. PMID: 7615809. <https://doi.org/10.1172/jci118045>
- Conti P., Ronconi G., Caraffa A., Gallenga C.E., Ross R., Frydas I., Kritas S.K. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. *Journal of Biological Regulators and Homeostatic Agents*. 2020 Mar 01; 34(2):327-31. PMID: 32171193. <https://doi.org/10.23812/conti-e>
- Brunton L.L., Parker L., Blumenthal D.K., Buxton I.L.O. Goodman and Gilman's Manual of Pharmacology and Therapeutics. New York: McGraw-Hill Medical, 2008:446-47.
- Amici C., Di Caro A., Ciucci A., Chiappa L., Castilletti C., Martella V., Decaro N., Buonavoglia C., Capobianchi M.R., Santoro M.G. Indomethacin has a potent antiviral activity against SARS coronavirus. *Antivir Ther* 2006;11(8):1021-30. PMID: 17302372. <https://pubmed.ncbi.nlm.nih.gov/17302372/>
- <https://hospitalhealthcare.com/covid-19/indomethacin-has-a-positive-impact-on-covid-19-symptoms>.
- Brunton L.L., Parker L., Blumenthal D.K., Buxton I.L.O. Goodman and Gilman's Manual of Pharmacology and Therapeutics. New York, NY: McGraw-Hill Medical; 2008: 446-7.
- Day M. Covid-19: ibuprofen should not be used for managing symptoms say doctors and scientists. *BMJ*. 2020 March 17; 368: m1086. <https://doi.org/10.1136/bmj.m1086>
- Gupta R., Misra A. Contentious issues and evolving concepts in the clinical presentation and management of patients with COVID-19 infection with reference to use of therapeutic and other drugs used in co-morbid diseases (Hypertension, diabetes, etc.). *Diabetes Metab Syndr*. 2020; 14(3): 251-4. PMID: 32247213. <https://doi.org/10.1016/j.dsx.2020.03.012>
- Updated: WHO now doesn't recommend avoiding ibuprofen for COVID-19 symptoms. <https://www.sciencealert.com/who-recommends-to-avoid-taking-ibuprofen-for-covid-19-symptoms>.
- Chmiel JF, Konstan MW, Accurso FJ, Lymp J, Mayer-Hamblett H, VanDevanter DR, Rose LM, Ramsey BW, Assessment of Induced Sputum in Cystic Fibrosis Study Group. Use of ibuprofen to assess inflammatory biomarkers in induced sputum: implications for clinical trials in cystic fibrosis. *J Cyst Fibros*. 2015 Nov; 14(6): 720-6. PMID: 25869324. <https://doi.org/10.1016/j.jcf.2015.03.007>
- Zhang W., Zhao Y., Zhang F., Wang Q., Li T., Liu Z., Wang J., Qin Y., Zhang X., Yan X., Zeng, and Zhang Sh. The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): the perspectives of clinical immunologists from China. *Clin Immunol*. 2020 Mar 25; 214: 108393. PMID: 32222466. <https://dx.doi.org/10.1016%2Fj.clim.2020.108393>
- Lucas S. The Pharmacology of Indomethacin. *Headache*. 2016 Feb 11; 56(2): 436-46. <https://doi.org/10.1111/head.12769>
- Draper M.P., Martell R.L., Levy S.B. Indomethacin-mediated reversal of multidrug resistance and drug efflux in human and murine cell lines overexpressing MRP, but not P-glycoprotein. *Br. J. Cancer*. 1997; 75(6): 810-5. PMID: 9062400. <https://doi.org/10.1038/bjc.1997.145>
- Vane J.R., Botting R.M. Mechanism of action of anti-inflammatory drugs. *Scand J Rheumatol Suppl*. 1996;102:9-21. PMID: 8628981. <https://doi.org/10.3109/03009749609097226>
- Tegeer I., Pfeilschifter J., Geisslinger G. Cyclooxygenase-independent actions of cyclooxygenase inhibitors. *FASEB J*. 2001 Oct; 15(12):2057-72. PMID: 11641233. <https://doi.org/10.1096/fj.01-0390rev>
- Amici C., La Frazia S., Brunelli C., Balsamo M., Angelini M., Santoro M.G. Inhibition of viral protein translation by indomethacin in vesicular stomatitis virus infection: role of eIF2 $\alpha$  kinase PKR. *Cell. Microbiol*. 2015 Sep;17(9):1391-404. PMID: 25856684. <https://dx.doi.org/10.1111%2Fcmi.12446>
- Hoppmann R.A., Peden J.G., Ober S.K. Central nervous system side effects of nonsteroidal anti-inflammatory drugs. Aseptic meningitis, psychosis, and cognitive dysfunction. *Arch. Intern. Med*. 1991 Jul;151(7):1309-13. PMID: 2064481

## INDOMETHACIN & SARS-COV-2: ПЕРСПЕКТИВИ КЛІНІЧНОГО ЛІКУВАННЯ СТАНОМ ЗАПАЛЕННЯ. Огляд

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**Актуальність.** Важкий гострий респіраторний синдром (Severe acute respiratory syndrome – SARS) характерний для пандемії, званої SARS-related coronavirus 2 (SARS-CoV-2), або COronaVirus Disease-19 (COVID-19), і викликаній невідомим сімейством РНК-вірусу – коронавірусом (SARS-COV-2). Фенотип може варіювати від безсимптомного до блискавичного цитокинового шторму, який призводить до поліорганної недостатності та смерті. Відомо, що індометацин має здатність пригнічувати реплікацію РНК і ДНК вірусів.

**Мета:** обговорити можливість клінічного лікування запалення, викликаного SARS-COV-2, за допомогою індометацину.

**Матеріали та методи.** Аналіз наукових публікацій в міжнародній електронній наукометричній бази даних PubMed за ключовими словами за період 1991-2020рр. Зіставлення з клінічними випадками.

**Результати.** Інтерлейкіни (IL), інтерферони (IFN) і метаболіти, утворені ферментом циклооксигеназою (COX 1 / COX 2), активні проти деяких РНК-вірусів. Експерти розділили інфекцію SARS на три фази (фази 1, 2, 3) в залежності від ступеня тяжкості. У фазі 3 спостерігається «цитокиновий шторм» через сильне запалення, яке може пошкодити органи і навіть привести до летального результату. Індометацин може пригнічувати синтез простагландинів, вироблюваних циклооксигеназою, пригнічує реплікацію коронавіруса і цитокиновий шторм і знижує вираженість гіперзапального стану. Індометацин є потужним інгібітором ГРВІ CoV-2.

**Висновок.** Індометацин, що має противірусну активність, можна вважати безпечним і ефективним для профілактики і лікування коронавірусної інфекції.

**Ключові слова:** індометацин, COVID-19, SARS-COV 2, запалення.

## ИНДОМЕТАЦИН И SARS-COV-2: ПЕРСПЕКТИВЫ КЛИНИЧЕСКОГО ЛЕЧЕНИЯ СОСТОЯНИЯ ВОСПАЛЕНИЯ. Обзор

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**Актуальность.** Тяжелый острый респираторный синдром (Severe acute respiratory syndrome – SARS) характерен для пандемии, называемой SARS-related coronavirus 2 (SARS-CoV-2), или COronaVirus Disease-19 (COVID-19), и вызванной неизвестным семейством РНК-вируса – коронавирусом (SARS-COV-2). Фенотип может варьировать от бессимптомного до молниеносного цитокинового шторма, который приводит к полиорганной недостаточности и смерти. Известно, что индометацин обладает способностью подавлять репликацию РНК и ДНК вирусов.

**Цель:** обсудить возможность клинического лечения воспаления, вызванного SARS-COV-2, с помощью индометацина.

**Материалы и методы.** Анализ научных публикаций в международной электронной наукометрической базе данных PubMed по ключевым словам за период 1991-2020рр. Сопоставление с клиническими случаями.

**Результаты.** Интерлейкины (IL), интерфероны (IFN) и метаболиты, образованные ферментом циклооксигеназой (COX 1 / COX 2), активны против некоторых РНК-вирусов. Эксперты разделили инфекцию SARS на три фазы (фазы 1, 2, 3) в зависимости от степени тяжести. В фазе 3 наблюдается «цитокиновый шторм» из-за сильного воспаления, которое может повредить органы и даже привести к летальному исходу. Индометацин может угнетать синтез простагландинов, вырабатываемых циклооксигеназой, подавляет репликацию коронавируса и цитокиновый шторм и снижает выраженность гипервоспалительного состояния. Индометацин – мощный ингибитор SARS CoV-2.

**Вывод.** Индометацин, обладающий противовирусной активностью, можно считать безопасным и эффективным для профилактики и лечения коронавірусної інфекції.

**Ключевые слова:** индометацин, COVID-19, SARS-COV 2, воспаление.

## REFRACTORY FUNGAL VAGINITIS TREATED BY TOPICAL AMPHOTERICIN B. Review

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**Abstract.** Vaginitis is a common problem for women regarding a worldwide health challenge with many side effects. Vaginitis is among the most visiting to gynecology clinics. About 75% of all reproductive women had at least one fungal vaginitis infection in their life, and more than 40% will have two or more than two. *Candida* spp is the most prevalent in fungal vaginitis, while reports for unusual fungi were observed as mucor spp.

Amphotericin B (AmB) belongs to the polyene group has a wide spectrum in vitro and in vivo antifungal activity. All of the known available formulas of AmB are administrated via intravenous injection to treat severe systemic fungal infections, while the development of the topical formula of AmB is still under preliminary development including topical vaginal AmB.

Due to the revealing of antimicrobial-resistant fungi in recent years, this study explains the role of topical AmB in treating refractory fungi vaginitis that may not a response to other drugs reported in many cases that may help researchers to develop new effective formula of AmB regarding fungal vaginitis.

**Keywords:** fungal vaginitis, antifungal drugs, topical Amphotericin B, Amphotericin B formula.

**Introduction.** Most common women had vaginitis at a certain period in their lives that associated with different ages [1]. Vaginitis is the most predominant infection in the female genital tract and is recognized among women in the primary health centers and gynecology departments. vaginal infections alone account for more than 10% of patients visit women's health units [2]. Vaginitis is a common term that refers to inflammation of the vaginal wall that caused by one of three causes: fungal yeast infections, trichomoniasis, and bacterial vaginosis [3].

**Amphotericin B (AmB)** is an ancient agent used over many decades in treating various fungal infections clinically in the human [4]. Low fungal resistance and broad-spectrum antifungal activities are the most valuable pharmaceutical characters encourage continuous usage of AmB [5].

This study highlights the topical efficacy of AmB to treat fungal vaginitis depending on searches and case report studies for rare cases regarding vaginitis.

**Advantages of topical AmB.** There are many advantages to using AmB as a topical treatment of dermatophytosis. Firstly, discover new drugs or

modification old one will participate to increase the available limited number of antifungal drugs [6]. Secondly, topical preparations are much less costly than orally administered antifungal drugs and cause minimal adverse side effects [7-8].

Third, the application of the topical formula of AmB considers more safety to use and will not produce clinically relevant serum levels of AmB [8-9]. Fourth, the quality of patient life will increase if new drugs improved to cure infectious lesions in a short time [6].

**Topical usage of AmB for refractory fungal vaginitis.** Topical modern applications of AmB provide a promising way of fungal treatment to reduce the adverse effects of intravenous usage of AmB [4]. Five interesting articles have been revealed the role of topical AmB to treat refractory fungal vaginitis (table 1).

Phillips was prepared topical vaginal suppositories of 50 mg AmB showed successful management of 70% of ten women with non-albicans *Candida* vaginitis after given nightly for 14 days. Suppositories medicine is also revealed less local side effects and well-tolerated [10].

Table 1

Topical AmB used in vagina							
Ref	Fungi type	NO. patients	AmB Dose	AmB formula	Treatment duration	Result	Year
10	non-albicans <i>Candida</i>	32	50 mg nightly	AmB vaginal suppositories	14 days	70% of women treated	2005
11	<i>Candida krusei</i>	1	3% daily	AmB vaginal gel	14 days	symptoms is resolved	2016
12	<i>Mucor species</i>	1	3% 5 g daily	AmB	7 weeks	disappearing of symptoms, culture-ve	2001
13	<i>Candida glabrata</i>	3	100 mg once daily	AmB lubricating jell	2 weeks	significant improvement	2001
14	<i>Candida glabrata</i>	1	100 mg once Nightly	AmB vaginal applicator	14 days	negative culture after 2 weeks	2003

Chamorro and his colleagues studied the topical formulation of amphotericin 3 % to treat *Candida krusei* vaginitis was developed by combining amphotericin B deoxycholate with lubricating jelly Aquagel®. Propyleneglycol was used for lubricant incorporation the intravaginal formulation was given daily for 14 days; the patient had resolved her symptoms [11].

Sobel mentioned that 3 % topical amphotericin B 5 g daily has been used to treat a rare case of vaginitis caused by *Mucor* species in healthy woman, *Mucor* vaginitis appeared refractory resistant to flucytosine as well as an azole. The treatment outcome, disappearing of symptoms and she has culture-negative [12].

White et al. found that Flucytosine (one gram) and AmB (100 mg) prepared in lubricating jell were used per vagina once daily to treat vaginal *Candida glabrata* had failed to respond to antifungals therapy, significant improvement, clinical resolving and negative microbiological culture observed after 2 weeks treatment [13].

Shann and Wilson: the treatment of *Candida glabrata* resistant to antifungal drugs isolated from vaginal swabs by using vaginal applicator nightly, for 14 days of amphotericin 100 mg plus flucytosine 1 g in Aquagel. Her symptoms had resolved and culture results for *Candida glabrata* were negative [14].

**Vaginitis prevalence and management.** Vaginitis is a widely distributed problem among women mainly associated with discomfort. Symptomatic vaginitis accorded for millions of clinical visits yearly [15]. Vaginitis is a global problem that not just women, but also families and communities.

It may have dangerous complications such as ectopic pregnancy, chronic pelvic pain, abortion, infertility, increasing of HIV transmission, low-birth weight infant. For these reasons, true prevention and management of vaginitis is great important [16].

*Candida albicans* is responsible for 65-90 % of vaginal *Candida* species infections, and non-*albicans* *Candida* species are responsible for up to 30 % [17]. From 1,740 symptomatic patients, vaginal candidiasis observed in 32,8 % [18].

*Candid* spp is the leading cause beyond infectious vaginitis; it colonizes about twenty percent of vagina that considered important opportunistic fungal microbe [19]. Vulvovaginal candidiasis (VVC) is the second most commonly reported form of infectious vaginitis. However, the totality of fungal microbes found within the vagina has been grossly underestimation. On the other hand, we have large information about bacteria that harboring vaginal milieu [19].

**General features of AmB.** Amphotericin B (AmB) is an ancient agent used over many decades in treating various fungal infections clinically in the human. Opportunistic systemic fungal infection considered the most common type of fungal infection mainly treated by AmB [4].

At present, many studies focused on the topical preparation of AmB as eye drop [20] or gel [20] or

solution [21] or as nanoparticles drug [22]. However, treatment with topical AmB may not always give satisfying results as with ordinary forms of this drug in the treatment of fungal infection, while some topical applications of AmB gave performing outcomes with complete healing especially in certain cases not responded to conventional therapy.

The topical formula of AmB to treat fungal vaginitis give good results as mentioned in the previous studies, so developing this formula is necessary due to the appearance of drug-resistant fungi implicated in vaginitis.

## CONCLUSION

Vaginitis is one of the most common problems associated with discomfort and low quality of life in women that may make women under serious complications like ectopic pregnancy and abortion. Topical AmB formulas are a promising way to develop effective management of the refractory fungal vaginitis.

Using AmB in modern branches and new applications is demanded because AmB is a potential antifungal agent with rare resistance, as well as its broad-spectrum activity toward many fungal infections, more studies about topical AmB vaginal formulas are recommended.

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## REFERENCES

1. Kimberly A Workowski, Stuart Berman. Sexually transmitted diseases treatment guidelines. Centers for Disease Control and Prevention (CDC). 2015; 64: 1-137. Access mode: <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6403a1.htm>
2. Karaer A., Boylu M., Avsar A.F. Vaginitis in Turkish women: symptoms, epidemiologic-microbiologic association // Eur J Obstet Gynecol Reprod Biol. 2005; 121: 211-5. doi: 10.1016/j.ejogrb.2004.11.030. PMID: 16054964
3. Karasz A., Anderson M. The vaginitis monologues: women's experiences of vaginal complaints in a primary care setting // Soc Sci Med. 2003; 56 (5): 1013-21. doi: 10.1016/s0277-9536(02)00092-8. PMID: 12593874.
4. AL-Khikani F.H., AL-Janabi A.A. Topical Amphotericin B formulas: Promising new application // International Journal of Medical Science and Current Research. 2019; 2: 187-96. Access mode: <http://www.ijmscr.com/issue/archive>
5. Lanternier F., Lortholary O. Liposomal amphotericin B: what is its role in 2008? // Clinical Microbiology and Infection. 2008; 14 (4): 71-83. DOI: 10.1111/j.1469-0691.2008.01984.x
6. Scorzoni L., de Paula E. Silva A.C., Marcos C.M., Assato P.A., de Melo W.C., de Oliveira H.C., Costa-Oriandi C.B., Mendes-Giannini M.J., and Fusco-Almeida A.M. Antifungal therapy: new advances in the understanding and treatment of mycosis // Frontiers in Microbiology. 2017; 8: 1-23. <https://doi.org/10.3389/fmicb.2017.00036>

7. Crawford F., and Hollis S. Topical treatments for fungal infections of the skin and nails of the foot // Cochrane Database of Systematic Reviews. 2007; 3: CD001434. doi: 10.1002/14651858.CD001434.pub2.
8. Hay R. Therapy of skin, hair and nail fungal infections // Journal of Fungi. 2018; 4 (3): 99. <https://dx.doi.org/10.3390%2Fjof4030099>
9. Pendleton, R. A., and Holmes IV, J. H. Systemic absorption of amphotericin B with topical 5 % mafenide acetate/amphotericin B solution for grafted burn wounds: Is it clinically relevant? // Burns. 2010; 36 (1): 38-41. <https://doi.org/10.1016/j.burns.2009.04.009>
10. Phillips A.J. Treatment of non-albicans Candida vaginitis with amphotericin B vaginal suppositories // American journal of obstetrics and gynecology. 2005; 192 (6): 2009-12. <https://doi.org/10.1016/j.ajog.2005.03.034>
11. Chamorro-de-Vega E., Gil-Navarro M.V., Perez-Blanco J.L. Treatment of refractory Candida krusei vaginitis with topical amphotericin B // Medicina clinica. 2016; 147 (12): 565-6. doi: 10.1016/j.medcli.2016.06.029.
12. Sobel J.D. Vaginal mucormycosis: a case report // Infectious diseases in obstetrics and gynecology. 2001; 9: 117-8. doi: 10.1155/S1064744901000205.
13. White D.J., Habib A.R., Vanthuyne A., Langford S., Symonds M. Combined topical flucytosine and amphotericin B for refractory vaginal Candida glabrata infections // Sexually transmitted infections. 2001; 77 (3): 212-3. <https://doi.org/10.1136/sti.77.3.212>
14. Shann S., Wilson J. Treatment of Candida glabrata using topical amphotericin B and flucytosine // Sexually transmitted infections 2003; 79 (3): 265-6. <https://doi.org/10.1136/sti.79.3.265-a>
15. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2014. Atlanta (GA): U.S. Department of Health and Human Services; 2015. Access mode: <https://wonder.cdc.gov/wonder/help/STD/STDSurv2014.pdf>
16. Centers for Disease Control and Prevention. Genital/vulvovaginal candidiasis statistics. Retrieved March 27, 2012. Available from: <http://www.cdc.gov/disease/candidiasis/genital/statistics.html>
17. Kennedy MA, Sobel JD. Vulvovaginal candidiasis caused by non-albicans Candida species: new insights // Curr Infect Dis Rep. 2010; 12(6): 465-70. <https://www.researchgate.net/deref/http%3A%2F%2Fdx.doi.org%2F10.1007%2Fs11908-010-0137-9>
18. Gaydos CA, Beqaj S, Schwebke JR, Lebed J, Smith B, Davis TE, Fife KH, Nyirjesy P, Spurrell T, Furgerson D, Coleman J. Clinical validation of a test for the diagnosis of vaginitis // Obstetrics and gynecology. 2017; 130 (1): 181. <https://dx.doi.org/10.1097%2FAOG.0000000000002090>
19. Bradford LL, Ravel J. The vaginal mycobiome: A contemporary perspective on fungi in women's health and diseases // Virulence. 2017; 8 (3): 342-51. doi: 10.1080/21505594.2016.1237332.
20. Morand, K., Bartoletti, A. C., Bochot, A., Barratt, G., Brandely, M. L., and Chast, F. Liposomal amphotericin B eye drops to treat fungal keratitis: physico-chemical and formulation stability // International Journal of Pharmaceutics; 2007; 344 (1-2): 150-3. doi: 10.1016/j.ijpharm.2007.04.028.
21. Trasmonte M.V., Jiménez J.D., Santiago M.Á., Gálvez E., Jerez V., Pérez D., and Rubio J. A. Association of topical amphotericin B lipid complex treatment to standard therapy for rhinomaxillary mucormycosis after liver transplantation: a case report // In Transplantation Proceedings. 2012; 44 (7): 2120-3. doi: 10.1016/j.transproceed.2012.07.081
22. Sanchez D.A., Schairer D., Tuckman-Vernon C., Chouake J., Kutner A., Makdisi J., Friedman J.M., Nosanchuk J.D. and Friedman A.J. Amphotericin B releasing nanoparticle topical treatment of Candida spp. in the setting of a burn wound // Nanomedicine: Nanotechnology, Biology and Medicine. 2014; 10 (1): 269-77. doi: 10.1016/j.nano.2013.06.002.

## МІСЦЕВЕ ЛІКУВАННЯ РЕФРАКТЕРНОГО ГРИБКОВОГО ВАГІНІТУ АМФОТЕРИЦИНОМ В.

### Огляд

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**Резюме.** Вагініт є загальною проблемою для жінок у всьому світі, з багатьма побічними ефектами. Вагініт – одна з найбільш розповсюджених причин відвідування гінекологічних клінік. Близько 75% всіх репродуктивних жінок мали принаймні одну грибову вагінітну інфекцію у своєму житті, а понад 40 % – дві або більше двох. Candida spp є найбільш поширеним при грибовому вагініті, тоді як повідомлення про незвичні гриби спостерігалися як тусог spp.

Амфотерицин В (AmB) відноситься до полієнової групи, має широкий спектр *in vitro* протигрибової активності. Всі відомі доступні формули AmB вводяться за допомогою внутрішньовенної ін'єкції для лікування важких системних грибових інфекцій, тоді як розробка актуальної формули AmB ще знаходиться на стадії попередньої розробки, включаючи місцевий вагінальний AmB.

Завдяки виявленню антимікробних стійких грибів в останні роки, це дослідження пояснює роль актуального AmB у лікуванні рефрактерного грибового вагініту, що може не відповідати на інші препарати, про які повідомляється у багатьох випадках, які можуть допомогти дослідникам розробити нову ефективну формулу AmB щодо грибового вагініту.

**Ключові слова:** грибовий вагініт, протигрибові препарати, амфотерицин В місцево, формула амфотерицину В.

## МЕСТНОЕ ЛЕЧЕНИЕ РЕФРАКТЕРНОГО ГРИБКОВОГО ВАГИНИТА АМФОТЕРИЦИНОМ В. Обзор

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**Резюме.** Вагинит является распространенной проблемой для женщин во всем мире, со многими побочными эффектами. Вагинит является одним из самых распространенных причин посещения гинекологических клиник. Около 75% всех репродуктивных женщин имели, по крайней мере, одну грибковую инфекцию вагинита в своей жизни, и более 40 % – две или более двух. *Candida spp* является наиболее распространенным при грибковом вагините, в то время как сообщения о необычных грибах наблюдались как *miscog spp*.

Амфотерицин В (AmB) относится к полиеновой группе, обладает широким спектром противогрибковой активности *in vitro* и *in vivo*. Все известные доступные формулы AmB вводятся посредством внутривенной инъекции для лечения тяжелых системных грибковых инфекций, в то время как разработка местной формулы AmB все еще находится в стадии предварительной разработки, включая актуальный вагинальный AmB.

В связи с выявлением устойчивых к противомикробным препаратам грибов в последние годы, это исследование объясняет роль местного AmB в лечении рефрактерного грибкового вагинита, который во многих случаях может не реагировать на другие препараты, о которых сообщалось, что может помочь исследователям разработать новую эффективную формулу AmB в отношении грибкового вагинита.

**Ключевые слова:** грибковый вагинит, противогрибковые препараты, амфотерицин В местно, формула амфотерицина В.

## ANATOMY OF THE SPINAL CORD'S BLOOD SUPPLY. Review

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**Relevance.** The traditional scheme of blood supply to the spinal cord, formed in the 60-70s of the last century, does not correspond to the pathogenesis of many neurological disorders of the spinal cord. There is also a discrepancy in terminology: the names of arteries found in surgical and neurological works do not correspond to the names of the International Anatomical Nomenclature. Therefore, today this issue needs further analysis.

**Objective:** to summarize the information of different authors on the number of spinal branches and their branches, topography, blood supply to each segment of the spinal cord, to analyze the individual variability of sources of blood supply to the spinal cord.

**Materials and methods.** Analysis of scientific publications in the international electronic scientometric database PubMed by keywords for the period 2000-2018. and comparing these data with the imaginations of 1760-1993.

**Results.** The idea of the structural organization of the blood supply to the spinal cord has changed. With modern data, intracranial sources, namely: anterior and posterior spinal arteries, blood supply to the true cervical spinal cord, and the rest of the department - lower cervical, thoracic, lumbar, sacral and coccygeal - blood supply from extracranial sources, and they exist in this area segmental branches of the aorta. Nowadays, extracranial sources are considered the main in the blood supply to the spinal cord. It is now known that the anterior and posterior spinal arteries are intermittent and cannot provide blood supply to the spinal cord, as previously thought. The general plan of arterial blood supply of a spinal cord can be presented in the form of set of pools of front and back radical (radiculomedullary) arteries. The anterior radicular arteries are 4-8, and the posterior 15-20, respectively, along the spinal cord in its ventral and dorsal departments the same number of arterial pools is formed. There are anastomotic connections between these pools, which are not always functionally complete. Each of these basins is supplied by a separate radiculomedullary artery. Each such artery feeds not one but several segments of the spinal cord. The number and levels of approach to the spinal cord of radiculomedullary arteries, especially the anterior ones, differ significantly in individual variability. The perception of vascularization of the cervical spinal cord was analyzed. At different times, information about the number of arteries that supplied blood to this department differed significantly: in 1760 it was believed that it was 31 arteries; and in 1882-1939 - only 7; in 1943 - 27, in 1958 - 6-8; in 1958 - 7-10; in 1961-1963 - 5-8; in 1966-1973 - 5; in 1993 - 1-2 arteries. Such different information about spinal cord vascularization is the result of significant individual variability.

**Conclusions.** Incomplete current knowledge about the blood supply to the spinal cord is the cause of unresolved problems of etiology, pathogenesis and clinical course of spinal ischemic strokes, including cervical localization. The existing terminological confusion regarding the names of the arteries that supply blood to the spinal cord, in particular its cervical region, is explained by the significant variability of the radiculomedullary arteries of this zone in terms of number, diameter and location. Due to the existence of arterio-venous anastomoses, arterial myelobulbar anastomoses, adjacent areas of blood supply in this area, theft phenomena are formed and distant foci of ischemia appear, including both the spinal cord and the brain. Therefore, in order to make an angiotopic diagnosis, it is necessary to take into account not only anatomical, but also physiological and pathophysiological aspects of regulation and compensation of cerebral circulation.

**Keywords:** spinal cord vascularization, cervical region, radiculo-medullary arteries.

**Relevance.** Acute cerebrovascular disorders often lead to irreversible neurological damage, which is accompanied by the development of persistent disability of the patient [16]. According to statistics, spinal strokes account for about 1% of all (cerebral and spinal strokes together), and some authors believe that the exact prevalence of spinal strokes is not known for sure [3, 16]. This pathology is quite rare, and, despite the urgency of the problem, the clinical and morphological features of spinal strokes are insufficiently studied. The fact that spinal strokes occur much less frequently than cerebral strokes can be explained by the small size of

the spinal cord, the large number of arterial anastomoses and the lower prevalence of atherosclerotic lesions of the spinal arteries [18]. Cervical strokes cause the most severe neurological disorders: from muscle weakness to paraplegia or tetraplegia, depending on the level and depth of the lesion, and in cases of ischemia to the brainstem - rapid death.

Nowadays, the sources of blood supply to the spinal cord are generally described; these data are set out in textbooks on normal anatomy. However, the literature data on a detailed description of the blood supply to different parts of the spinal cord and the distribution

of intravascular vessels of the spinal cord, taking into account individual variability, is extremely small, and these sources date mainly to the 60-70s of last century.

So the blood supply to the spinal cord is an extremely important and urgent problem, but at the same time little studied, which requires further study.

Objective of this work was to summarize the information of different authors on the number of spinal branches and their branches, topography, blood supply to each segment of the spinal cord, to analyze the individual variability of spinal blood supply sources.

## MATERIALS AND METHODS

Analysis of scientific publications in international electronic scientometric databases by keywords for the period 2000-2018. and comparing these data with the imaginations of 1760-1993.

## RESULTS

From the XVIII and almost to the end of the XIX century in anatomy there was a stable idea of the blood supply to the spinal cord, which will be set out in almost all anatomical textbooks, both domestic and foreign [1, 10, 11, 15, 20]. According to traditional notions, the main sources of spinal cord supply are three arterial trunks: unpaired anterior and paired posterior spinal arteries (branches of the vertebral arteries of the subclavian artery - right and left). The anterior and posterior spinal arteries run along the spinal cord in the rostrocaudal direction. Blood in these arteries comes from the intracranial part of the right and left vertebral arteries and then flows continuously along the entire spinal cord. Posterior spinal arteries start from the posterior inferior cerebellar artery (branches of the intracranial part of the spinal artery) or directly from the intracranial part of the spinal artery, encircle the medulla oblongata, enter the spinal canal and go to the posterior surface of the spinal cord, which include the posterior radicles. The right and left anterior spinal arteries depart from the corresponding vertebral artery at the level of the anterior edge of the occipital foramen, on the anterior surface of the medulla oblongata at the level of the pyramids, and form an unpaired anterior spinal artery, which goes down on the anterior surface of the spinal cord.

An additional source of blood supply to the spinal cord were considered to be the radicular arteries (branches of the spinal arteries), which correspond to each segment of the spinal cord, have the same diameter and increase blood flow in the main longitudinal arteries.

But the traditional scheme of blood supply to the spinal cord did not correspond to the pathogenesis of many neurological disorders of the spinal cord. Gradually, under the influence of the work of many scientists [2, 4, 5, 13], our ideas about the structural organization of the blood supply to the spinal cord change. According to current data, intracranial sources, namely the anterior and posterior spinal arteries, supply blood only to the upper

cervical segments of the spinal cord, and the remaining segments - lower cervical, thoracic, lumbar, sacral and coccygeal - are supplied from extracranial sources, namely from the branches of the subclavian artery, branches of the aorta. Thus, in our time, extracranial sources are considered the main in the blood supply to the spinal cord [2, 4, 5, 13].

Despite the identification of priority sources of blood supply to the spinal cord, there are still many controversial and unresolved issues regarding the detailed description of its blood supply, especially the cervical region. These specific issues concerning the number of spinal branches and their branches, topography, blood supply to each segment of the spinal cord, etc., are the most important in clinical practice, because they determine the development and features of pathological lesions of certain parts of the spinal cord. Little is known about the individual variability of spinal blood supply sources. There is still a terminological discrepancy between the names of the arteries that supply blood to the spinal cord: the names of the arteries found in surgical and neurological works do not correspond to the names of the International Anatomical Nomenclature [8].

The founders of the modern concept of blood supply to the spinal cord are A. Adamkiewicz (1881-1882) and H. Kadyi (1886, 1889), who in the nineteenth century from other points of view covered the blood supply to the spinal cord. A. Adamkiewicz first proved that the number of spinal arteries is reduced and does not correspond to the number of segments of the spinal cord. The author called these arteries «spinal», and their branches - anterior and posterior spinal arteries. According to A. Adamkiewicz, 3 to 13 anterior spinal arteries are defined. The largest diameter of the anterior spinal (root) artery in the caudal part of the spinal cord, the author called A. magna spinalis. Later, this artery became known after the author who described it - Adamkevich's artery.

H. Kadyi proposed the terms «radicular» branches instead of anterior and posterior spinal arteries, so as not to confuse them with the anterior and posterior spinal arteries. In the modern anatomical nomenclature (São Paulo, 1997) and its Ukrainian standard (2001), the anterior and posterior root branches and the segmental cerebral artery are distinguished among the branches of the spinal arteries. The term «radiculomedullary arteries» dominates in textbooks and scientific literature on neurology. The segmental cerebral artery, as a branch of the spinal artery, is practically not described in the modern anatomical and neurological literature. According to some data, the segmental cerebral artery connects with the anterior spinal artery [8]. According to other data, the segmental artery is part of the posterior root of the spinal nerve and is involved in the blood supply to the spinal cord.

Subsequent work has shown that the main source of blood supply to the spinal cord are the root arteries,

and their number is much smaller than the number of segments of the spinal cord.

The radicular arteries in the upper parts of the spinal cord are branches of the spinal branches that extend from the spinal artery (right and left). In the lower parts of the spinal cord, the root branches are branches of the spinal branches coming from the posterior intercostal arteries (segmental branches of the thoracic aorta), lumbar arteries (segmental branches of the abdominal aorta), and lateral sacral and iliac-lumbar arterial arteries. Due to the fact that in embryogenesis the spinal cord lengthens more slowly than the spinal column grows, the segmental arteries enter the spinal cord above the level of their departure from the aortic trunk.

Determine the anterior and posterior radicular arteries. The anterior radicular arteries accompany the anterior radicles of the spinal nerve, and the posterior - respectively, the posterior radicles of the spinal nerve.

It is proved that the radicular arteries approach the spinal cord not symmetrically, but more often from the left side. The anterior radicular arteries enter the spinal cord along its length alternately: then left, then right. Symmetrical approach of two such arteries to one spinal segment is rare. Much more often these arteries enter the spine and spinal cord on the left side. This is due to the left location of the aorta. With a right-sided location, the artery, crossing the spine in front, goes a long way.

The radicular arteries, although they accompany the nerve roots, most of them are not directly involved in the blood supply to the spinal cord. According to H. Kadui, only 25% of the radicular arteries passing into the spinal canal are involved in the blood supply to the spinal cord.

The beginning of the radicular artery can be said only from the moment of entry of the spinal branch into the subdural space.

The radicular arteries are divided into several types:

- part of the radicular arteries end within the root of the spinal nerve,
- part of the radicular arteries ends in the dura mater (these are the dura mater arteries),
- part of the radicular arteries joins the pial vascular system (vascular system of the soft membrane of the spinal cord),
- part of the radicular arteries that reach the spinal cord, merge with the anterior and posterior spinal arteries and take a major part in the blood supply to the spinal cord.

Those radicular arteries that reach the spinal cord and merge with the anterior and posterior spinal arteries are referred to in the neurology literature as the radicular-spinal or radiculomedullary arteries. These arteries play a major role in the blood supply to the spinal cord.

The anterior radicular arteries are smaller, but they are larger in diameter. As a rule, it is determined from 2 to 27 anterior radicular arteries (often 4-8) and from 6 to 28 posterior radicular arteries (more often 15-20). In the cervical anterior radicular arteries in most cases there are

3, in the upper and middle parts of the thoracic 2-3 thin anterior radicular arteries are determined, and the lower thoracic, lumbar and sacral spinal cord receive blood from 1 to 3 anterior radicular arteries [6].

The largest anterior radicular (radiculomedullary) artery (up to 2 mm in diameter) is the lumbar thickening artery (Adamkevich's artery), which supplies blood to the lower half of the thoracic segments, lumbar, sacral and coccygeal segments. The level of discharge of this artery from the posterior intercostal or lumbar artery is variable. In 75% of people it varies from the level of Th8 to L2.

The anterior root branches provide blood supply 4/5 of the cross section of the spinal cord.

The anterior parts of the spinal cord are mainly supplied with blood by 6-8 radicular (radicular or radiculomedullary arteries). They depart from certain arteries, but the level and direction of discharge may vary. C3 departs from the spinal artery. C6 - usually from the deep carotid artery, C8 - from the rib-neck trunk. In 10% at the lower cervical level there is no anterior radicular artery.

The largest anterior radicular arteries are identified in the middle cervical spinal cord (cervical thickening artery, or Lazort's artery) and in the inferior thoracic or upper lumbar region (lumbar thickening artery, or Adamkevich's artery). In 15-16% the large anterior radicular artery which accompanies an anterior root of L5 or S1 (Deproz-Gotteron's artery) is defined. There are variants when the upper additional anterior radicular artery accompanying one of the thoracic roots is determined [9].

The areas of entry of the radicular arteries into the spinal canal are quite variable. For example, the Adamkiewicz artery may enter the spinal canal at the level of the 9th thoracic to 2 lumbar vertebrae.

Although the posterior radicular arteries are larger, they are less powerful and play a smaller role in the blood supply to the spinal cord as a whole.

At the level of C7-8 - T1 posterior radicular arteries are absent in 10%.

Each anterior and posterior radicular arteries, approaching the surface of the spinal cord, are dichotomously divided into ascending and descending branches, which are widely anastomosed with similar branches above and below the radicular arteries. These anastomoses below the upper cervical segments on the anterior surface of the spinal cord in the anterior middle slit form the anterior anastomotic tract - anterior spinal artery, and on the posterior surface, respectively, in the posterior lateral sulcus form posterior anastomotic tracts - posterior spinal arteries [9].

Along the anastomotic tracts, areas with oppositely directed blood flow are defined, which are located, as a rule, in the place of division of the main trunk of the radicular artery into ascending and descending branches [9]. Thus, the anterior and posterior spinal arteries, on

the one hand, are longitudinal anastomoses between the respective ascending and descending branches of the anterior and posterior radicular arteries, and on the other hand, due to their branches connecting the anterior and posterior spinal arteries, form transverse anastomoses between the anterior and posterior radicular arteries.

Numerous transverse anastomoses are formed between the anterior and posterior spinal arteries, which together form the crown of the spinal cord on the cross sections [13].

From the anterior spinal artery or anterior anastomotic tract, depart the central branches that supply 80% of the spinal cord: anterior and lateral cords, anterior and lateral horns, the base of the posterior horns, the central area around the central canal and partially the posterior cords. The posterior spinal arteries (posterior anastomotic tracts) supply blood to the posterior horns, most of the posterior cords, and the posterior lateral cords. The areas of the spinal cord that are located in critical areas on the border of the anterior and posterior spinal arteries are the worst supplied with blood: this is the base of the posterior horns, the substance around the central canal, the posterior adhesion.

The posterior spinal arteries form a large number of branches that anastomose with each other and with the anterior spinal artery. These branches are sometimes called coronal, they surround the perimeter of the spinal cord and are involved in the formation of the coronary artery plexus, or pialic network. The branches of this plexus, as well as the coronary arteries enter the substance of the spinal cord and provide blood supply to the marginal parts of the white matter.

According to modern notions, the blood supply system of the spinal cord consists of two parts: vertical (along the spinal cord) and transverse. The vertical part of the spinal cord blood supply system is formed by the anterior and posterior spinal arteries, which are often called anterior and posterior spinal arteries in the literature, and branches of the spinal branches from the subclavian artery system and segmental branches from the thoracic and abdominal aorta.

It is now known that the anterior and posterior spinal arteries are intermittent and cannot provide blood supply to the spinal cord, as previously thought. The anterior spinal artery is formed at the level of C1-C2 due to the fusion of the right and left anterior spinal arteries. Below this level along the anterior surface of the spinal cord, the anterior spinal artery is an anastomotic tract, which is formed by the corresponding, rather large in diameter, anterior radicular branches (from 2 to 5-6).

At the level of the segment where the anterior spinal artery is approached by the anterior radicular (radiculomedullary) arteries, blood flow has the opposite direction: along the ascending branch - cranial, and along the descending branch - caudal. The anterior spinal artery is represented by a continuous trunk in the cervical and lumbosacral spinal cord, and at the level of

the mid-thoracic artery this artery is interrupted. Below the cervical segments, the paired posterior spinal arteries are less developed and are formed from 10-23 posterior radicular arteries, representing a continuation of the posterior radicular arteries, which are oriented upwards and downwards. Below the cervical segments due to incomplete fusion of the posterior radicular arteries in some areas the lumen of the posterior spinal arteries may be absent.

Blood from the spinal arteries steadily flows only to the upper cervical segments. Further, due to the decrease in their diameter, increase in blood flow resistance, decrease in pulse blood pressure, intermittent lumen, blood flow in the cerebral arteries is almost absent. Therefore, starting from the cervical segments, the source of blood supply to the spinal cord is the radicular arteries [14].

In the vertical part of the spinal cord blood supply system there are two hemodynamic arterial pools: upper and lower. The upper basin (or spinal subclavian), which supplies blood segments C1-Th2, includes the anterior and posterior spinal arteries, which supply blood C1-C4 segments; and 3-7 radicular arteries that supply blood to the rest of the cervical and 2-3 upper thoracic segments. The lower pool (or aortic pool) supplies blood to the lower segments of Th3-S5, which receive blood from the segmental branches of the aorta.

On a cross section define three pools, or zones of blood supply, a spinal cord. The first zone is central, occupies a middle position and is the largest in terms of blood supply. The central zone includes the anterior horns, anterior gray adhesions, adjacent areas of the lateral and anterior cords. The central zone is supplied with blood by paired furrowed branches from the anterior spinal artery. Each of these arteries supplies blood only to the corresponding half (right or left) of the cross section of the spinal cord. The second zone of blood supply is dorsal, formed by the immersion branches of the posterior spinal arteries. The dorsal arterial area of blood supply includes the posterior horns and posterior cords. The third arterial zone is a periodic situation, on the cross section of the spinal cord it performs the marginal sections of the transitional and lateral canals. This area receives blood supply from the immersion branches and from the existing areas of the perimedullar network (vase-crown network) and the pial vascular network.

Depending on the number of root arteries, there are two types of spinal cord blood supply: main and placental. A small number of radicular arteries - 3-5 anterior and 6-8 posterior - determines the main type of blood supply to the spinal cord. The main type determines the extreme variant, when only 3-4 anterior radicular arteries supply blood to the cervical and upper thoracic segments of the spinal cord, and the lower thoracic, lumbar, sacral and coccygeal segments are supplied with only one anterior radicular artery - Adamkevich's artery. The main type of blood supply to the spinal cord is determined in 48%. There is a variant when the spinal cord below Th1 - Th2

is supplied with blood by only one Adamkevich artery (12%). In the presence of placer type, the radicular arteries supplying blood to the spinal cord are much larger - 6-12 anterior and 22 or more posterior [9]. Each anterior radicular artery supplies blood to several adjacent segments of the spinal cord, so in the presence of circulatory disorders in one of these arteries, blood flow is relatively easily compensated. The loose type of blood supply is determined in 42%. The type of blood supply to the spinal cord is genetically determined and affects the formation of the spinal arteries in the lower parts of the spinal cord. In the presence of the main type of blood supply to the spinal cord, the anterior spinal artery in the lower basin is formed by branches of one radicular artery (20%) or two radicular arteries: upper accessory radicular artery.

In the pool of blood supply to the spinal cord, both in the vertical and horizontal planes, critical areas are identified in which there is a low level of arterial blood flow.

According to modern ideas, the anterior and posterior spinal arteries are not continuous vessels, and blood flow in these vessels may have the opposite direction, which leads to the formation along the long axis of the spinal cord border areas of blood supply (levels C4, Th4, Th9 - L1).

Along the spinal cord in the longitudinal direction there are also areas of reduced blood circulation, located on the border of the basins of the radicular (radiculomedullary arteries). These critical areas are variable in size because it determines the significant individual variability in the number of radicular arteries and the level of their entry into the spinal cord. Most often, such critical areas include the upper thoracic segments, the area of the spinal cord above the lumbar thickening and the terminal part of the spinal cord.

From the point of view of conditions of hemodynamics, in longitudinal arterial vessels allocate other critical zones of blood supply of a spinal cord. Thus, in the process of anatomical examination it was noticed that the smallest diameter of the anterior spinal artery is mainly found in the middle between the lateral tributaries (anterior root). Proponents of Adamkevich's theory of the direction of blood flow in the longitudinal spinal arteries believe that it is in these narrow areas of the artery are opposite directions of blood flow. This hypothetical zone of zero pressure in the area of relative narrowing of the vascular bed, apparently, is a functional watershed between two adjacent radiculo-medullary basins. Such areas are called «border» or «adjacent» zone. This area includes both part of the longitudinal arterial tract and the area of the spinal cord that supplies them with blood. These border areas are especially vulnerable to circulatory failure.

K.J. Zulch identified an intermediate zone at the level of Th4-Th9 between the upper and lower arterial basins, which is insufficiently supplied with blood by the anterior root artery, which goes together with the roots of

Th6-Th7. He localized a particularly threatening «critical zone» as the boundary between the vertebral and aortic basins in the Th4 segment. Other critical areas are located between the upper and lower tributaries in the cervical thickening C3-C4 and between the lower thoracic and upper lumbar tributaries - approximately L1-2.

Unlike K.J. Zulch, some authors have noted that softening is most common in areas of spinal cord thickening. According to C. Fazio (1965), at the level of the cervical segments, the danger zone is the area C3-C4. According to J. Corbin (1960), ischemic strokes are localized in the areas of cervical and lumbosacral thickenings.

Given the great variability in the location of arterial sources, it is impossible to insist on the stability of border areas and strictly link them to certain spinal segments. The only exception is the adjacent area between the two main remote arterial basins: the vertebral-subclavian and aortic. This zone is quite permanent. This is evidenced by experimental data, which showed that when excluding the aortic basin, the lower limit of the filling of the vascular system is at C8-Th3. According to K. Jellinger, the boundary zone between the two main sections of human blood flow is not at the level of Th4, as suggested by K. J. Zulch (1954), and above - at C8-Th 1-2.

From the point of view of physiology of dynamics of blood circulation, for a spinal cord there are two opposite concepts about the greatest defeat of pools of blood supply and localization of secondary changes at condition of vascular insufficiency. Proponents of one concept believe that the most commonly affected areas with insufficient vascularization are the thoracic segments in the vertical plane. In the transverse plane - these are the areas between the central and peripheral areas of blood supply to the spinal cord. The founders of another theory, on the contrary, believe that the most vulnerable are areas that are heavily supplied with blood and functionally active in conditions of reduced arterial blood flow. In the vertical plane, these are the areas of cervical and lumbosacral thickenings. In the transverse plane, this is the central area that is most functionally active.

Thus, the blood supply to the spinal cord is carried out mainly by a reduced number of segmental arteries. G. Lazorthes called this phenomenon a «summation» of the radicular arteries.

Therefore, the general plan of arterial blood supply of a spinal cord can be presented in the form of set of pools of front and back radical (radiculomedullary) arteries. If we keep in mind that on average the anterior root arteries are 4-8, and the posterior 15-20, then, respectively, along the length of the spinal cord in its ventral and dorsal departments the same number of arterial pools is formed. There are anastomotic connections between these pools, which are not always functionally complete. Each of these basins is supplied by a separate radiculomedullary artery. Each

such artery feeds not one but several segments of the spinal cord. The number and levels of approach to the spinal cord of radiculomedullary arteries, especially the anterior ones, differ significantly in individual variability [13].

According to estimates by K. Jellinger, who studied 700 drugs, the largest number of anterior root arteries passes to the cervical thickening at the height of C5-C7, slightly less - to the caudal thoracic segments (at the height of Th6-Th10). In the thoracolumbar region (Th10-L2), in the upper cervical segments (C3-C4) the number of drives is much smaller. The minimum part falls on the transitional cervical-thoracic region (C3-Th2) and the lower lumbar segments (L3-L4). Intraorganic vessels of the spinal cord, belonging to the basin of the anterior radicular arteries and anterior spinal artery, form the central part of the arterial system of the spinal cord and supply blood in the direction from the center to the periphery of the spinal cord area, which is 4/5 of its diameter. The remaining 1/5 of the spinal cord, located mainly in the marginal areas of white matter, feeds mainly on the perimedullar vascular network, which in turn receives blood from the posterior radicular and posterior spinal arteries (they are always larger than the anterior, but they are almost in diameter twice as thin as its previous counterparts) [13].

Counting the frequency of active root arteries at the level of individual segments of the human spinal cord (400 drugs), K. Jellinger noticed that the lowest frequency of both anterior and posterior arteries occurs at the level of C3-Th1-2. On this basis, he suggested that the C8-Th1-2 segments often represent the anatomical boundary between the two basins - the subclavian and aortic.

The number of functioning coronary arteries is very variable. It should be noted that variability is available within individual vertical basins. In the same case, in the lower arterial basin there may be 1-2 anterior radicular (radiculomedullary) arteries, while in the upper basin there may be much more [13].

M. Maliszewski, having studied 50 preparations of the spinal cord and assessing the location, diameter and ligaments of blood vessels, identified 7 vascular areas: upper cervical area (C1-C3), middle cervical area (C4-C5), cervical thickening (C6-C8), upper thoracic zone (Th1-Th3), middle thoracic zone (Th4-Th7), thoracolumbar thickening (Th8-L4) and lumbosacral zone (L5-Co1-3).

Богородинський Д.К., Скоромець О.А. розглядаються два основних шляхи кровопостачання спинного мозку, відкриваючи від дуги аорти. Верхній басейн із хрестовими та іншими провідними гілок підключичного артерії (а. Vertebralis, а. Cervicalis ascendens et profundus, intercostalis suprema). The radicular branches of these arteries provide nourishment to all cervical and first or second upper thoracic segments of the spinal cord (upper arterial pool of the spinal cord). The second way of blood supply is provided by

segmental branches of an aorta and internal iliac arteries (aa. Intercostales posteriores, subcostalis, lumbales, lumbalis ima, ilio-costalis, sacralis lateralis et mediana). This lower arterial basin of the spinal cord includes all its segments below Th2. In some cases, at the level of the lower basin there is only one anterior radiculomedullary artery - Adamkevich's artery. This demonstrates that the isolated G. Lazorthes and J.L. Corbin third, the so-called intermediate, arterial zone does not always occur. In addition to these anatomical findings, the feasibility of dividing the blood supply to the spinal cord into two basins is also dictated by clinical considerations. At disturbance of blood circulation in the top arterial pool tetraparesis usually arises, but quite often at the same time stem symptoms (myelobulbar defeats) can join also. The clinical sign of circulatory disorders in the lower basin is lower paraparesis.

Let's focus in more detail on the blood supply to the cervical spinal cord.

According to classical notions, the cervical spinal cord is supplied with blood by branches from the subclavian artery basin, namely: spinal artery - paired (branches of the right and left subclavian arteries), ascending carotid artery - paired (branches of the right and left thyroid-cervical trunk from the subclavian trunk from deep carotid and the highest intercostal arteries - paired (branches of the right and left costal-cervical trunk from the subclavian arteries).

Sources of blood supply to the cervical spinal cord are divided into two groups: intracranial and extracranial.

Intracranial sources are the anterior spinal artery. The right and left anterior spinal arteries depart from the intracranial part of the corresponding vertebral artery at the level of the anterior edge of the occipital foramen, exit the skull and on the anterior surface of the medulla at the pyramids connect at an acute angle and form an unpaired anterior spinal artery. the middle of the furrow. Thus, on the anterior surface of the lower part of the brain stem and upper cervical segments, a vascular rhombus or vascular circle is formed, the upper sides of which form parts of the vertebral arteries at the junction with the main artery, and the lower sides are the right and left cerebral arteries in front of them. connection. This vascular circle was named by Zakharchenko MA «Circulus arteriosus bulbaris». The lower part of the vascular rhombus is located either on the ventral surface of the medulla oblongata or on the anterior surface of the cervical segment. And from the vessels of the lower part of this circle depart the so-called «sulcal» arteries, which supply blood not only to the structures of the medulla oblongata, but also the upper cervical segments. Given this, the described arterial complex, it might be correct to call «circulus arteriosus myelobulbaris».

According to Adamkiewicz, thin branches depart from each vertebral artery, which go to the ventral surface of the medulla oblongata obliquely down and medially. Adamkiewicz called these branches vertebrospinal.

They combine with each other either within the medulla oblongata, or more often at the height of the 2nd and 3rd cervical segments. This is how the only anterior spinal artery is formed here. G. Lazorthes emphasizes that the anterior spinal artery at the upper cervical level is always much thinner than depicted in earlier manuals. In addition to the anterior spinal artery, from the intracranial part of both vertebrae, sometimes from the inferior cerebellar arteries, originate two posterior spinal arteries that run along the posterior surface of the superior cervical segments [13].

Blood is thought to flow evenly from the right and left vertebral arteries to the corresponding anterior spinal arteries, but studies have shown that the contribution of one of the vertebral arteries is greater.

On direct X-rays, the anterior spinal artery is first oblique, then it is located strictly along the midline to the C4 vertebra, where it connects with the ascending branch of the radicular (radiculomedullary) artery of the cervical thickening. Another radiculomedullary artery is often present at this level. In lateral images, the anterior spinal artery runs along the posterior surface of the arches and the tooth of the second cervical vertebra, below - along the posterior surface of the vertebral bodies.

During the upper cervical segments, the anterior spinal artery retains its lumen, so it directly supplies blood to the upper cervical segments of the spinal cord. In addition to the upper cervical segments of the spinal cord, the anterior spinal arteries also supply blood to the anterior part of the medulla oblongata, the pyramids, the lower part of the spinal cord, the posterior longitudinal bundle, and the sublingual nerve nucleus.

Sometimes in section C1-C4, an additional anterior radicular artery is identified, which goes along with the third or fourth anterior radicle.

Extracranial sources are spinal branches (rr.spinales), which depart from the transverse (cervical) part of the vertebral arteries, paired deep cervical, ascending cervical and superior intercostal arteries.

As a rule, there are no anterior root arteries in the area of the first cervical segments. However, the posterior carotid arteries from the vertebral arteries are suitable for the upper cervical segments. At the level of the cervical

region, the large anterior root arteries most often depart from the deep artery of the neck, rather than from the vertebral arteries, as previously thought.

Thus, the first upper cervical segments receive blood from the anterior spinal artery. The lower cervical segments (C4-C8) and the upper thoracic segments (Th1-Th3) are supplied with blood by two unpaired root arteries, which go to the right or left and depart either from the vertebrae or from the ascending carotid artery and rib-carotid trunk.

The cervical thickening has a dense network of blood capillaries, especially in the deep part of the anterior horns. At the level of cervical thickening, each motor motoneuron is surrounded by a three-dimensional capillary network. Experimental studies have shown that the highest blood flow velocity is determined in the area of cervical and lumbosacral thickenings (VI Klevtsova, 1968).

The number of anterior and posterior radicular arteries in the cervical spinal cord is quite variable (Table 1) [13].

From the rib-cervical trunk to the left or right there is a rather large branch, which supplies blood to the lower segments of the cervical spinal cord. This artery has the shape of a «hairpin», it connects with the ascending branches to the anterior spinal artery. In some cases, there is a variant of blood supply to the spinal cord by the anterior radicular (radiculomedullary) artery extending from the thyroid-cervical trunk [13].

F. Schweighofer on 23 corpses by injection of the vessels of the cervical spinal cord found that the anterior radicular (radiculomedullary) artery only in one case departed from the spinal artery. In other cases, it departed from the deep artery of the neck. Occasionally, he found a large radiculomedullary artery (up to the cervical thickening) that receded directly from the left subclavian artery.

One of those arteries that reach the cervical thickening sometimes has a larger diameter than the others. As a rule, such an artery is located lower than the others, departing from the radicular artery of the thyroid-cervical trunk, which goes together with the 7th or 8th radicles; sometimes it passes with the 6th and 7th cervical radicles; less often this artery is a branch of the vertebral or deep

**The number of anterior radicular arteries in the cervical spinal cord, according to the literature**

Автор	Year	The average number of arteries	Number of spinal cord samples
A. Haller	1760	31	6
A. Adamkiewicz	1882	7	13
F. Suh, L. Alexander	1939	7	15
М. І. Левантовський	1943	27	48
G. Lazorthes	1958	6-8	62
L. Gillian	1958	7-10	20
J. Corbin	1961	5-8	5-8
T. Mannen	1963	5-8	235
K. Jellinger	1966	5	303
D. Bogorodinsky, O. Skoromets	1973	5	78
F. Schweighofer	1993	1-2	23

carotid artery. Lazorthes proposed to call this artery «artery of cervical thickening», by analogy with the artery of lumbar thickening described by Adamkevich. This comparison is based on the clinical importance of the artery, although it is not valid for the diameter and frequency with which it occurs.

However, the term has not been fixed in the literature. European and domestic scientists call it differently: as a Lazort artery, as a cervical thickening artery, as a large cervical radiculomedullary artery, as a C7-radicular artery, but always emphasizing its clinical significance [7, 12, 13, 19, 21].

Japanese researchers on sectional material (87 corpses) found a total incidence (88.5%) of a special artery, which she called the «additional ascending artery of the neck», which originates from the subclavian artery behind the anterior ladder muscle and lies on the brachial plexus [21]. This study is consistent with their previous studies, in which this artery was detected in 86% of cases. The discharge and topography of this artery presented in this study correspond to the vessels previously described as the «unknown branch» or «deep ascending artery of the neck.» On 154 sides (88.5%), the additional ascending artery of the neck extended from the subclavian artery behind the anterior ladder muscle. Among them: this artery departed as a separate artery on 105 sides, or as a common trunk with a rib-neck trunk on 31 sides, with a transverse artery of the neck on 16 sides, or with them both on 2 sides. On 69 sides of 174 sides (39.7%) the additional ascending artery of the neck formed a common trunk with a rib-neck trunk medially from the anterior ladder muscle or behind it on 44 sides (25.3%), or with a transverse artery of the neck ( type B or C, according to Outi) behind the anterior ladder muscle or laterally from it on 20 sides (11.5%). Rarely, an additional ascending artery of the neck formed a common trunk with the rib-neck trunk or with the transverse artery of the neck medially from the muscle or behind it (3 sides, 1.7%), or from the thyroid-neck trunk (2 sides, 1.1%). This study showed that the additional ascending artery of the neck gives branches to the 6th and / or 7th cervical roots of the humeral plexus. These branches are considered as characteristic or important arteries departing from the original artery [21].

Thus, the literature on the blood supply to the spinal cord is small, outdated and contradictory [17], which requires further study. And the current terminological confusion regarding the names of the arteries that supply the spinal cord, including the cervical region [7, 12, 13, 19, 21], is due to the significant variability of radiculomedullary arteries in this area in number, diameter and location [13]. And this is also a serious problem that needs to be solved.

## CONCLUSIONS

1. Literature data covering in detail the current aspects of blood supply to various parts of the spinal cord

are insufficient, and these sources date mainly to the 60-70s of last century. These gaps are the cause of unresolved problems of etiology, pathogenesis and clinical course of spinal ischemic strokes, including cervical localization, and need further study.

2. The current terminological confusion regarding the names of the arteries that supply blood to the spinal cord, in particular its cervical region, is explained by the significant variability of the radiculomedullary arteries of this area in number, diameter and location. And this is also a serious problem that needs to be solved.

3. To make an angiotoxic diagnosis it is necessary to take into account not only anatomical but also physiological and pathophysiological aspects of regulation and compensation of cerebral circulation, because in connection with the existence of arteriovenous anastomoses in this area, arterial myelobulbar anastomoses, robbery phenomena are formed and distant foci of ischemia appear, including both the spinal cord and the brain.

Конфлікт інтересів: відсутній /

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## REFERENCES

- [Human anatomical atlas: translation from the 8th English edition. - 3rd edition / F. Martini. – K.: Medicine, 2018: 128 p. [in Ukrainian]. URL: [https://znannia.com.ua/product/anatomichnii\\_atlas\\_lyudini\\_pereklad\\_z\\_8go\\_angliis4kogo\\_vidannya\\_angliis4koyu\\_ukrains4koyu\\_rosiis4koyu\\_ta\\_latins4koyu\\_movami\\_frederik\\_martini](https://znannia.com.ua/product/anatomichnii_atlas_lyudini_pereklad_z_8go_angliis4kogo_vidannya_angliis4koyu_ukrains4koyu_rosiis4koyu_ta_latins4koyu_movami_frederik_martini)
- Badalyan L.O. [Neuropathology. Textbook]. – M.: Academy, 2007: 400 p. [in Russian]. URL: <https://gist.github.com/anonymous/3b87d7333a618a83f64a0bfb2313a10>
- Vilensky BS. [Emergencies in neurology: A guide for physicians]. – S.-Pb.: FOLIANT, 2004: 512 p. [in Russian].
- Guzeva VI. [Handbook of Pediatric Neurology]. – M.: MIA, 2009: 640 p. [in Russian]. URL: <https://www.booksmed.com/nevrologiya/2625-rukovodstvo-po-detskoy-nevrologii-guzeva.html>
- [Pediatric neurology. Textbook in 2 vol. / ed. O.S Petrukhin]. – M.: GEOTAR-Media, 2018: 272 p. [in Russian]. URL: <http://www.geotar.ru/lots/NF0009635.html>
- Zhulev NM, Badzgaradze Yu. D., Zhulev SN. [Osteochondrosis of the spine. Manual for physicians]. – S.-Pb.: Lany, 1999: 592 p. [in Russian]. URL: <https://www.booksmed.com/nevrologiya/2827-osteohondroz-pozvonochnika-zhulev.html>
- Lutsik AA, Kazantsev VV, Bondarenko G.Yu., Peganov AI. [Vascular myelopathy, caused by compression or stenosis abnormal vertebral artery, supplying the thickening of the cervical spinal cord] // Medicine in Kuzbass. 2014;13 (2): 55-62 [in Russian]. URL: <http://mednauki.ru/index.php/MK/issue/viewIssue/114/114>
- [International anatomical nomenclature: Ukrainian standard: Textbook] / ed. II Bobryk, VG Koveshnikov.

- К.: Zdorov`ya, 2001: 327 p. [in Ukrainian]. URL: <http://library.univer.kharkov.ua/OpacUnicode/index.php?url=/notices/index/IdNotice:261458/Source:default#>
9. [Nervous diseases: a textbook for medical students] / ed. MM Odina. – S.-Pb.: SpetsLit, 2014: 526 p. [in Russian]. URL: <https://speclit.su/image/catalog/978-5-299-00587-5/978-5-299-00587-5.pdf>
  10. Netter F. [Atlas of human anatomy] / Ed. N.O. Bartosh, L.L. Kolesnikov. – M.: GEOTAR-Media, 2007: 624 p. [in Russian]. URL: <http://www.medlan.samara.ru:8006/images/1-349.jpg>
  11. Olson T. R. [Atlas of human anatomy. A.D.A.M.] – M.: Med. lit., 2012.2012: 504 p. [in Russian]. URL: <https://kim.by/catalog/anatomiya-i-fiziologiya/atlas-anatomii-cheloveka.-a.d.a.m.>
  12. Popelyansky Ya. Yu. Orthopedic neurology (vertebroneurology). A guide for doctors. – M: MEDpress-inform, 2011: 672 p. [in Russian]. URL: <https://www.mmbook.ru/catalog/newrologija/neurologyo/108371-detail>
  13. Skoromets OA, Skoromets GP, Skoromets TO, Thyssen TP Spinal angioneurology. A guide for doctors. – M: MEDpress-inform, 2003: 608 p. [in Russian]. URL: <https://www.mmbook.ru/catalog/newrologija/neurologyo/101737-detail>
  14. Tishevskoy IA. Anatomy of the Central Nervous System: A Textbook. - Chelyabinsk: Izd-vo YuUrGU. 2000: 131 p. [in Russian]. URL: [http://pedlib.ru/Books/4/0137/4\\_0137-1.shtml](http://pedlib.ru/Books/4/0137/4_0137-1.shtml)
  15. Cherkasov VG, Kravchuk S.Yu. Human anatomy: textbook. – Vinnytsia: Nova Kniga, 2018: 640 p. [in Ukrainian]. URL: <https://books.google.com.ua/books?id=tNmuCQAAQBAJ&printsec=frontcover&hl=ru#v=onepage&q&f=false>
  16. Aljishi M., Abernethy D. Spinal Cord Infarction // The New Zealand Medical Student Journal. 2015; 20: 18-21.
  17. Bergui M., Ventili G., Ferrio F.M., Daniele D.R. Spinal Cord Ischemia due to Vertebral Artery Dissection // Neuroradiol J. 2005 June 1; 18: 390-4. <https://doi.org/10.1177%2F197140090501800318>
  18. Sherman P. M., Gailloud P. Artery of the Cervical Enlargement Originating from the Inferior Thyroid Artery: An Angiographic Observation // Journal of Vascular and Interventional Radiology. 2004; 15 (6): 648-50. [https://doi.org/10.1016/S1051-0443\(07\)60341-8](https://doi.org/10.1016/S1051-0443(07)60341-8)
  19. Sobotta: Anatomie des Menschen. Der komplette Atlas in einem Band / Herausgegeben von R. Putz und R. Rabst. – Urban & Fischer, 2007: 830 p. URL: <https://lib.eu/book/750446/a04ad5?regionChanged>
  20. Su W.-D., Ohtsuka A., Taguchi T., Murakami T. Typology of the Arteries in the Human Scalenus Region, with Special Reference to the Accessory Ascending Cervical Artery // Acta Med Okayama. 2000; 54 (6): 243-52. doi: 10.18926/AMO/32280.

## АНАТОМІЯ КРОВОПОСТАЧАННЯ СПИННОГО МОЗКУ. Огляд

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**Актуальність.** Традиційна схема кровопостачання спинного мозку, сформована у 60-70 роках минулого століття, не відповідає патогенезу багатьох неврологічних розладів з боку спинного мозку. Також є неузгодженість у термінології: назви артерій, що зустрічаються в роботах хірургічного та неврологічного напрямів, не відповідають назвам Міжнародної анатомічної номенклатури. Тому сьогодні це питання потребує додаткового аналізу.

**Мета:** узагальнити відомості різних авторів щодо кількості спинномозкових гілок та їх розгалужень, топографії, кровопостачання кожного сегменту спинного мозку, проаналізувати індивідуальну мінливість джерел кровопостачання спинного мозку.

**Матеріали та методи.** Аналіз наукових публікацій в міжнародній електронній наукометричній базі даних PubMed за ключовими словами за період 2000-2018рр. та співставлення цих даних з уявами 1760-1993 рр.

**Результат.** Змінилися уявлення про структурну організацію кровопостачання спинного мозку. Згідно сучасних даних, внутрішньочерепні джерела, а саме: передня та задні спинномозкові артерії, кровопостачають тільки верхні шийні сегменти спинного мозку, а решта сегментів – нижні шийні, грудні, поперекові, крижові та куприкові – кровопостачаються із позачерепних джерел, а саме від гілок підключичної артерії та сегментарних гілок аорти. В наш час позачерепні джерела вважаються основними в кровопостачанні спинного мозку. Сьогодні відомо, що передня та задні спинномозкові артерії є перервними і не можуть забезпечити кровопостачання спинного мозку, як про це думали раніше. Загальний план артеріального кровопостачання спинного мозку можна представити у вигляді сукупності басейнів передніх і задніх корінцевих (радикуломедулярних) артерій. Передніх корінцевих артерій 4-8, а задніх 15-20, відповідно, вздовж спинного мозку в його вентральному і дорсальному відділах утворюється таке ж число артеріальних басейнів. Між цими басейнами наявні анастомотичні зв'язки, які не завжди функціонально повноцінні. Кожен з цих басейнів постачається окремою радикуломедулярною артерією. Кожна така артерія живить не один, а кілька сегментів спинного мозку. Число і рівні підходу до спинного мозку радикуломедулярних артерій, особливо передніх, відрізняються значною індивідуальною мінливістю. Проаналізовано, як мінялися уявлення про васкуляризацію шийного відділу. В різні часи відомості про кількість артерій, які кровопостачали цей відділ, суттєво відрізнялися: у 1760 р. вважалося, що це 31 артерія; а у 1882-1939 рр. – всього 7; у 1943 р. – 27, у 1958 р. – 6-8; у 1958 р. – 7-10; у 1961-1963 рр. – 5-8; у 1966-1973 рр. – 5; у 1993 р. – 1-2 артерії. Такі різні відомості про васкуляризацію спинного мозку є наслідком значної індивідуальної мінливості.

**Висновки.** Неповнота сучасних знань про кровопостачання спинного мозку є причиною невирішеності проблем етіології, патогенезу та клінічного перебігу спінальних ішемічних інсультів, зокрема цервікальної локалізації. Існуюча термінологічна плутанина щодо назв артерій, які кровопостачають спинний мозок, зокрема його шийний відділ, пояснюється значною варіабельністю радикуломедулярних артерій цієї зони за кількістю, діаметром та місцем відходження. У зв'язку з існуванням у цій зоні артеріо-венозних анастомозів, артеріальних мієлобульбарних анастомозів, суміжних зон кровопостачання, утворюються феномени обкрадання та з'являються дистантні вогнища ішемії, що включають як спинний, так і головний мозок. Тому для постановки ангіотопічного діагнозу обов'язковим є врахування не тільки анатомічних, але й фізіологічних та патофізіологічних аспектів регуляції та компенсації спинномозкового кровообігу.

**Ключові слова:** васкуляризація спинного мозку, шийний відділ, радикуло-медулярні артерії

## АНАТОМИЯ КРОВΟΣНАБЖЕНИЯ СПИННОГО МОЗГА. Обзор

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**Актуальность.** Традиционная схема кровоснабжения спинного мозга, сформированная в 60-70 годах прошлого века, не соответствует патогенезу многих неврологических расстройств со стороны спинного мозга. Также есть несогласованность в терминологии: названия артерий, встречающиеся в работах хирургического и неврологического направлений, не соответствуют названиям Международной анатомической номенклатуры. Поэтому сегодня этот вопрос требует дополнительного анализа.

**Цель:** обобщить сведения разных авторов по количеству спинномозговых ветвей и их разветвлений, топографии, кровоснабжение каждого сегмента спинного мозга, проанализировать индивидуальную изменчивость источников кровоснабжения спинного мозга.

**Материалы и методы.** Анализ научных публикаций в международной электронной наукометрической базе данных PubMed по ключевым словам за период 2000-2018 гг. и сопоставление этих данных с представлениями 1760-1993 гг.

**Результат.** Изменились представления о структурной организации кровоснабжения спинного мозга. Согласно современным данным, внутричерепные источники, а именно: передняя и задние спинномозговые артерии, питают только верхние шейные сегменты спинного мозга, а остальные сегменты – нижние шейные, грудные, поясничные, крестцовые и копчиковые – кровоснабжаются внечерепными источниками, а именно от ветвей подключичной артерии и сегментарных ветвей аорты. В настоящее время внечерепные источники считаются основными в кровоснабжении спинного мозга. Сегодня известно, что передняя и задние спинномозговые артерии являются прерывистыми и не могут обеспечить кровоснабжение спинного мозга, как об этом думали раньше. Общий план артериального кровоснабжения спинного мозга можно представить в виде совокупности бассейнов передних и задних корешковых (радикуломедулярных) артерий. Передних корешковых артерий 4-8, а задних 15-20, соответственно, вдоль спинного мозга в его вентральном и дорсальном отделах образуются также же число артериальных бассейнов. Между этими бассейнами имеются анастомотические связи, не всегда функционально полноценные. Каждый из этих бассейнов снабжается отдельной радикуломедулярной артерией. Каждая такая артерия питает не один, а несколько сегментов спинного мозга. Число и уровни подхода к спинному мозгу радикуломедулярных артерий, особенно передних, отличаются значительной индивидуальной изменчивостью. Проанализировано, как менялись представления о васкуляризации шейного отдела. В разное время сведения о количестве артерий, кровоснабжающих этот отдел, существенно отличались: в 1760 считалось, что это 31 артерия; а в 1882-1939 гг. – всего 7; в 1943 – 27, в 1958 – 6-8; в 1958 – 7-10; в 1961-1963 гг. – 5-8; в 1966-1973 гг. – 5; в 1993г. – 1-2 артерии. Такие разные сведения о васкуляризации спинного мозга являются следствием значительной индивидуальной изменчивости.

**Выводы.** Неполнота современных знаний о кровоснабжении спинного мозга является причиной нерешенности проблем этиологии, патогенеза и клинического течения спинальных ишемических инсультов, в частности цервикальной локализации. Существующая терминологическая путаница относительно названий артерий, кровоснабжающих спинной мозг, в частности его шейный отдел, объясняется значительной вариабельностью радикуломедулярных артерий этой зоны по количеству, диаметру и месту отхождения. В связи с существованием в этой зоне артерио-венозных анастомозов, артериальных миєлобульбарных анастомозов, смежных зон кровоснабжения, образуются феномены обкрадывания и появляются отдаленные очаги ишемии, включающие как спинной, так и головной мозг. Поэтому для постановки ангиотопического диагноза обязательным является учет не только анатомических, но и физиологических и патофизиологических аспектов регуляции и компенсации спинномозгового кровообращения.

**Ключевые слова:** васкуляризація спинного мозгу, шийний відділ, радикуло-медулярні артерії.

## DIAGNOSIS AND TREATMENT OF COMBAT INJURIES OF THE HEART AND GREAT VESSELS. Review

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**Relevance.** According to the modern realities of hostilities in the East of Ukraine, the medical community has grown a request for information about the nature of the most dangerous defeats of the participants of the Joint Forces Operation (JFO) in Donbass.

**Objective:** analysis and generalization of the nature of heart injuries received during the hostilities in the East of Ukraine, the stages of medical support of such wounded.

**Materials and methods.** Analysis of scientific publications in scientific journals of Ukraine by keywords for the period 2014-2018.

**Results.** The nature of injuries among participants in the JFO has been analyzed. The first place is occupied by injuries of blood vessels with bleeding (60%), 2 - pneumothorax (34%), and 3 - airway obstruction (6%). All this can be combined and supplemented by damage to the nervous system and other organs. In the conditions of the modern war in Donbass, shrapnel injuries (50.5%), bullet wounds (25.3%) and closed injury (20.3%) are considered frequent types of injuries. The classification of heart injuries, clinical symptoms, the levels of support for such a wounded are described: first aid at the prehospital stage («golden minutes») on the battlefield, qualified medical assistance («golden hour»), specialized medical care in a hospital. Post-traumatic stress disorders have been described that last from one to 6 months and require complex treatment.

**Conclusion.** According to NATO's new military medical doctrine, «an effective and reliable medical support system contributes to maintaining the trust of the military and the general public in the army and its political leadership.»

**Key words:** combat trauma, injury to the heart and blood vessels, stages of medical support, treatment of the wounded.

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### MATERIALS AND METHODS

Analysis of scientific publications in scientific journals of Ukraine by keywords for the period 2014-2018.

### RESULTS

Heart injury is an injury to an organ caused by mechanical forces (a blow with a blunt or sharp object, an explosive wave, building materials, a fall from a height, a car accident, and a variety of weapons during hostilities).

In peacetime, injuries to the heart and great vessels are very rare, but in wartime, their number increases significantly [6]. Such injuries are extremely life-threatening and require immediate and qualified surgical care. Among the most dangerous lesions of the participants of the Joint Forces Operation (JFO) in Donbas, blood

vessel injuries with bleeding are in the first place (60%), pneumothorax is in the second place (34%) and airway obstruction is in the third place (6%) [3]. All this can be combined and supplemented by damage to the nervous system and other organs [10].

#### Terminology

In the conditions of modern war in Donbass the most frequent types of injuries are considered shrapnel lesions (50.5%), bullet wounds (25.3%), and closed injuries (20.3%) [5]. Closed heart injury is damage to the heart by a traumatic object that can occur under the action of various solids on the chest (fist, stone, wood, building materials, moving vehicles, earth or asphalt when falling from a height, steering wheel in a car accident) without significant skin damage covers. Blunt trauma leads to a heart attack, regardless of whether the skin is damaged. The slightest damage to the heart in blunt trauma is manifested only by molecular changes and is defined as a *cardiac commotio*.

Severe blunt trauma to the heart can have consequences similar to an acute myocardial infarction or be accompanied by a heart rupture. Blunt heart injury accounts for 70% of all injuries to this organ [9].

At *contusion* owing to the action of a traumatic subject, there are hemorrhages in a myocardium, under

Term	Definition
Closed heart injury: <ul style="list-style-type: none"> <li>• cardiac commotio</li> <li>• contusion</li> <li>• cardiorrhexis</li> </ul>	heart damage caused by a blunt object on the heart (compression, shock, fall from a height, car injury, blast wave) damage to heart structures at the molecular level  accompanied by partial tears and hematomas in the myocardium penetrating damage to the outer walls of the heart, heart septa or valves
Open heart injury: <ul style="list-style-type: none"> <li>• damaged by a bladed weapon</li> <li>• damaged by a firearm (gunshot wound to the heart)</li> </ul>	heart damage caused by bladed weapon or firearms  stabbed or cut heart wound (knife, finch, bayonet, bayonet, sharpener, etc.)  heart damage resulting from the action of firearms (bullet, fragment, shot)
Combined heart injury	Simultaneous damage to the heart and other organs (stomach, lungs, liver)
Polytrauma	Simultaneous traumatic injury to several body systems
Penetrating heart wound	Penetrates the heart cavity: <ol style="list-style-type: none"> <li>a) blunt wound, having only an input channel,</li> <li>б) perforated wound, having an entrance and an exit</li> </ol>
Nonpenetrating heart wound	Does not penetrate the heart cavity, but can injure the pericardium and myocardium

an epicardium or subendocardial. There may be ruptures of muscle fibers, bleeding from damaged coronary vessels. Hematoma can constrict the coronary artery with the development of acute myocardial infarction (up to 6%). Sometimes the intima of the coronary artery is damaged and local thrombosis occurs. Cardialgia of varying severity and arrhythmia may occur. The most severe closed heart injuries are accompanied by rupture of external or internal structures of the heart and account for up to 31% of all closed heart injuries [1]. With closed heart injuries, there is an underestimation of the severity of the lesion.

#### *Penetrating heart injuries*

When the heart is injured by a *bladed weapon* (knife, bayonet, bayonet, etc.) there is a stab or cut wound on the skin of the chest or abdomen, but the size of the external injury does not correlate with the severity of the heart itself. At heavy penetrating damages of heart and great vessels, there is bleeding into a pericardial cavity. This causes cardiac tamponade with the risk of developing acute heart failure (with a hemopericardium volume of 150-200 ml) or cardiac arrest (with a hemopericardium of 450-500 ml). In the presence of a wide source of blood from the pericardial cavity, there is a rapid massive blood loss with a clinical picture of internal bleeding and hemorrhagic shock.

A *gunshot wound* has either only an entrance or an entrance and exit hole on the outer skin. The absence of an exit hole indicates a blind injury to the body, but for the heart, it can be both blind and penetrating.

At the *combined trauma* of the heart, the lungs are most often damaged. Traumatic injury to other organs can greatly change the clinical picture of heart injury due to additional sources of bleeding, pneumothorax, increased traumatic shock. When several or all organs are damaged, *polytrauma* occurs, which is most common when falling from a height, or auto trauma, barotrauma by an explosive wave. In such cases, there

is also a risk of underestimation of damage to the heart and great vessels.

70% of battle casualty have bleeding limb blood vessels and need an immediate apply a tourniquet («*golden minute*»). For example, when a femoral artery ruptures, uncontrolled blood loss leads to hemorrhagic shock in 25 seconds. The peculiarities of the wounds in the modern war in eastern Ukraine are that among the wounded, mine, and explosion damage by spalls predominates simultaneously in many parts of the body. Because the victim may be unconscious and in the «*under the gun zone*», first aid can be catastrophically delayed and this leads to dangerous blood loss.

#### *Classification of heart injuries*

Heart damage is divided into injuries and closed trauma (commotio, contusion, and rupture). Heart injuries are penetrated and non penetrable, blind and through, knife and gunshot wounds, isolated and combined [3].

Bullet wound forms a wound canal, a zone of tissue necrosis, and a zone of molecular shock. A bullet (shard) can pull pieces of clothing into the wound canal. The entrance of a gunshot wound on a body sometimes happens considerably distant from a site of heart that does not promote early diagnosis.

In penetrating stab wounds to the heart, the entrance can also be distant from the projection of the heart. The cut edges of the wound fall off and adapt well, so there is almost no external bleeding.

Heart contusion is the result of a blunt object, so the external signs of injury may not correspond to the severity of heart damage and only after electrocardiographic examination can detect signs of acute myocardial infarction.

Occasionally, a blunt trauma, especially due to sudden braking of the car in a car accident, causes a rupture of the descending thoracic aorta at the site of its anatomical fixation by an arterial ligament. Damage to the main arteries and veins can accompany any heart injury.

The traumatic heart injury can include such damages:

- 1) outer walls of the heart;
- 2) septa of the heart (ventricular and atrial);
- 3) coronary vessels;
- 4) valvular apparatus of the heart;
- 5) conduction system of the heart;
- 6) great arteries and veins.

#### *Clinical symptoms*

With a heart injury, the patient's condition is severe or critical, so there is little time for examination, diagnosis, and first aid. The wounded may be conscious or unconscious. He has tachycardia, arrhythmia, and drops in blood pressure (weak pulse).

#### *First aid*

According to modern military medical doctrine, medical care is provided on a multilevel basis, which distinguishes pre-hospital and hospital stages [2,8].

The *pre-hospital stage* has a basic level, which includes first aid and pre-medical care, which in some cases is provided in the form of self- and mutual aid. This is the «golden moment» on which the life of the wounded may depend. On the battlefield, a certain sequence should be followed in the actions of fighters in the event of injuries:

- the first priority is to help the wounded,
- the second priority is to prevent new injuries,
- the third priority is to complete the combat mission.

Since the soldier may be in the area «under fire», the victim should be moved to the «zone of relative safety», which is not directly shot, and after first aid (tourniquet, bandage, hemostatic agent, analgesic, immobilization by improvised means) ensure immediate evacuation from the battlefield to a nearby battalion medical center or stabilization point for first aid by emergency specialists. This assistance may include transport immobilization with regular tires, administration of plasma substitutes, injection of an antibiotic to prevent early infection, and subcutaneous administration of tetanus toxoid (1.0 ml). The wounded with prolonged bleeding and critical blood loss are separated from others and evacuated to a military hospital first. For each victim get «Primary patient card (form 100/0)». Control and additional correction of these measures are continued during the immediate evacuation of the victim to the nearest hospital (inspection of the tourniquet and bandage, removal of foreign bodies from the upper respiratory tract, drainage of intense pneumothorax, anti-shock measures).

According to the head of the medical service of the Ministry of Defense of Ukraine Andriy Verba, in the first period of the anti-terrorist operation, there was a lack of equipment for the evacuation of the wounded and low quality individual first aid kit, which included an obsolete tourniquet, naflubin, and a bandage. The new first-aid kit (first level IFAK) includes 15 positions, among which there is a hemostatic (Cellos), a CAT or SOFT turnstile, a nasopharyngeal tube (the size of a fighter), a HALO occlusive dressing, a decompression needle to relieve

intense pneumothorax, a set of tablets (75 diclofenac mg, paracetamol 500 mg, ceftriaxone 500 mg), anti-burn hydrogel bandage, and also tactical scissors [2].

According to modern military medical doctrine, a «golden hour» is allocated, during which the wounded must be given first aid by a doctor or paramedic, and within 4-6 hours - qualified or highly specialized care. For patients with heart injuries, such care is almost always delayed.

#### *Qualified doctor's assistance*

In the conditions of hostilities in the East of Ukraine, qualified assistance in most cases is provided by the doctors of the medical company of the brigade. The severity of the patient's condition is explained by the presence of traumatic shock, acute internal bleeding, sometimes with cardiac tamponade, acute heart failure due to injury of the valve apparatus, heart rhythm disorders, as well as possible damage to neighboring organs, for example, lungs, liver, great arteries and veins, middle caliber (intercostal and internal mammary arteries). With a simultaneous injury to the lung, tense pneumothorax and severe breathing disorders can develop very quickly.

If the doctor examines the victim immediately after being wounded in the chest, then the first question to which he must answer himself - does the patient have a heart injury? To answer this question, one should be guided by Beck's triad: a wound in the projection of the heart, cardiac tamponade, internal bleeding. The clinical symptoms of this triad can be confirmed by examining the patient:

- 1) hypotension and tachycardia with a paroxysmal pulse, which becomes weak or disappears upon inhalation;
- 2) cyanosis and swelling of the cervical veins, if there is no hypovolemic syndrome (central venous pressure of about 150 mm Hg. Art.)
- 3) a large heart (percussion), weakened tones (auscultatory).

If a heart injury is suspected, it is necessary to organize careful, but rather, transportation of the victim to the nearest surgical department, and in combat conditions - to a deployed military mobile hospital, or a district (city) hospital, where reinforcement groups from among military surgeons take part in the treatment. This is the second level of qualified medical care, which should be carried out within 60 minutes after injury («golden hour»).

In the medical company of the brigade, or in local hospitals, triage and evacuation of casualties is a priority. Among them are the wounded with signs of external bleeding and the wounded with signs of internal bleeding, who are evacuated in the first place. The long-term effect of the tourniquet may result in irreversible ischemia of the limb; in such cases, it is forbidden to remove the tourniquet, even temporarily. These victims are evacuated secondarily, or a limb is amputated on the spot.

### Specialized medical care

This is the third level of surgical care that is now provided in one of three frontline multidisciplinary hospitals:

- 1) Military Medical Clinical Center of the Northern Region (Kharkov).
- 2) a military hospital in Dnipro,
- 3) Regional Clinical Hospital. I.I. Mechnikov (metro station Dnipro).

In these multidisciplinary hospitals and hospitals, the wounded are allocated, in need of previous intensive care, and who are given surgical care after stabilization. The wounded, who undergo surgery on urgent grounds, are sent to the operating room. Another group consists of those wounded who can be operated on for delayed indications: pulsating hematomas, arteriovenous fistulas, amputation of dead limbs. If possible, one should strive for early restorative methods of vascular treatment (end-to-end anastomosis).

If a patient is taken to a hospital or appropriate hospital with suspected heart injury, then he should be immediately submitted to the operating room, especially if there are symptoms of internal bleeding, cardiac tamponade and tension pneumothorax.

The necessary diagnostic procedures, such as: history, examination of the patient, determination of blood group and Rh belonging, laboratory tests, ECG and echocardiography should be performed without delaying surgical intervention. In the absence of a critical condition of the patient and doubts about the diagnosis, preoperative examination may include chest x-ray, ultrasound, abbreviated blood count, and ECG.

*Anamnesis.* Determine the mechanism of injury and localization of wounds, the period of time that has passed after the injury, external blood loss, the presence of hemoptysis, crying of the patient.

*Examination.* Find out the state of consciousness (fear, agitation, stupor, coma), the general condition of the patient (satisfactory, severe, agonal), skin color (pale, cyanosis), respiratory rate and the presence of hemoptysis, pulse rate and blood pressure level, intensity of heart sounds, splash blood in the pericardium, wheezing in the lungs. Palpate to check for subcutaneous emphysema (pneumothorax), percussion tympanitis, or dullness over the lungs (hemothorax). Significant enlargement of the liver may indicate severe heart failure or cardiac tamponade.

#### *Instrumental diagnostic methods*

The best of them should be considered ultrasound, which is atraumatic and gives maximum information in the shortest time. In patients with blunt trauma to the heart, electrocardiography can be of significant value. Chest radiography is also desirable, but in the horizontal position of the patient its value decreases.

Diagnostic puncture can be performed to diagnose hemopericardium, hemothorax and pneumothorax, if it does not delay the operation. Partial aspiration of blood

from the pericardium and air from the pleural cavity may temporarily improve hemodynamics. Liquid blood should not be aspirated from the pleural cavity, as this will increase bleeding, and during surgery this blood can be used for reinfusion without the need for group and rhesus affiliation.

Bronchoscopy and laparoscopy can be performed after cessation of bleeding from the heart and main vessels, or with symptoms of asphyxia.

Thoracoscopy for heart injuries is impractical, as it takes a long time and does not provide benefits in treatment.

Laboratory tests provide important information about the amount of blood loss (hemoglobin, hematocrit, blood protein), the state of its coagulation, blood type and rhesus affiliation.

#### *Treatment*

At injuries of heart and main arteries surgical treatment according to vital indications is always shown. 60-70% of deaths among OOS fighters were due to bleeding. In cases of heart attack due to blunt trauma, the victim is transported and treated according to the principles of acute myocardial infarction. The wounded man is intubated in the heart and transferred to artificial respiration. If necessary, support hemodynamics with sympathomimetics (dopamine, dobutamine), but do not raise blood pressure above the minimum allowable, so as not to increase bleeding. If in doubt about the choice of surgical access, it is best to use a left thoracotomy in the IV-V intercostal space. If necessary, this access can be extended to the right with a cross section of the sternum (branded access). Extended transverse access allows you to control all four chambers of the heart, the main vessels, both lungs and their pleural cavities.

Reaching the pericardial sac, the surgeon opens it wide along the phrenic nerve, sucks the liquid blood into a sterile vessel with an anticoagulant for reinfusion, which is performed by an anesthesiologist. Having established the location of the heart wound, the surgeon covers it with the finger of his left hand and stops further bleeding. When this is successful, further surgical action can be not forced, but give the anesthesiologist some time to stabilize hemodynamics and respiration. The surgeon applies sutures with his right hand (preferably with an atraumatic needle) and is tied by an assistant. Next, control other sources of bleeding (intercostal and internal thoracic arteries), detect and suture lung wounds, perform a sequential audit of all available tissues, remove blood clots. The wound is washed and drainage tubes are installed in each of the open pleural cavities and in the pericardium. The surgical wound is closed in layers. Intensive care and surgical treatment of concomitant lesions, reposition of bone fragments. If necessary, resort to re-surgical treatment of the wound to eliminate complications: hematomas, purulent swellings.

Almost all gunshot wounds end in suppuration, severe pain, osteomyelitis, vascular and nerve damage.

An untreated wound with a bullet or splinter, starting at six o'clock, causes purulent complications and sepsis. All combat wounds should be drained.

Combat injuries of the heart and blood vessels can be complicated by hemorrhagic shock, disseminated intravascular coagulation syndrome, general intoxication, renal and hepatic failure, acute cardiovascular failure, generalization of the infection with the transition to sepsis, the spread of infection to the vessel.

#### *Post-traumatic stress disorder (PTSD)*

The consequence of a favorable option for the treatment of wounded and injured during hostilities may be PTSD [4]. This is a delayed and prolonged reaction to an extreme traumatic event that is threatening or catastrophic. Constant companions of PTSD – depression and anxiety. In addition, psychologists pay attention to the following manifestations:

- flash backs – obsessive re-memories of extreme events that cause difficult emotional experiences, repeated nightmares about past events;
- avoidance of thoughts, conversations, places, events and people related to the injury;
- hyperactivity with sleep disorders, irritability, outbursts of anger, difficulty concentrating, constant expectation of a threat, excessive timidity;
- violation of social and professional adaptation.

Therefore, a patient with PTSD should be referred to a psychiatrist by a family or other physician. Also pay attention to the presence of tachycardia and shortness of breath. PTSD is a serious mental condition that occurs as a result of traumatic situations (participation in hostilities, violence or death). Not only the military but also members of their families, temporarily displaced persons and those forced to remain in a zone of military conflict are vulnerable to PTSD. Symptoms of PTSD can be manifested not only in the wounded, but also in other participants in hostilities, as a result of psychological stress.

PTSD lasts from one to 6 months and requires *comprehensive treatment*. Beta-blockers provide rapid anti-anxiety and vegetative-stabilizing effect without sedative effect. It is best to use bisoprolol, which has the highest beta-1 selectivity and no adverse effects on the respiratory system, peripheral circulation. Bisoprolol is soluble in both water and fats. It can be combined with antidepressants and statins [7]. Sertraline, paroxetine and psychotherapy are also effective.

In some cases, PTSD becomes chronic over several years with periods of wavy exacerbation [7]. Such patients become isolated and professionally incompetent, in communication with relatives they are capricious and dissatisfied, but easily come into contact with other participants in similar events. For qualified treatment of PTSD patients are referred to special rehabilitation centers.

## CONCLUSION

According to NATO's new military medical doctrine, «an effective and reliable medical care system helps to maintain the confidence of the military and the general public in the military and its political leadership».

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## REFERENCES

1. Belenky VA, Negodyuko VV, Mikhailusov RN. [Analysis of errors in the performance of primary surgical treatment of gunshot wounds of soft tissues] // *Surgery of Ukraine*. 2015; 1: 7-13. [in Russian]. URL: file:///C:/Users/%D0%A2%D0%B0%D1%82%D1%8C%D1%8F%D0%BD%D0%B0%20%D0%98%D0%B2%D0%B0%D0%BD%D0%BE%D0%B2%D0%BD%D0%B0/Downloads/KhU\_2015\_1\_3.pdf
2. Bondarevsky AO, Koval BM. [Levels of medical support of modern armed conflicts] // *Surgery of Ukraine*. 2015; 4: 7-13. [in Ukrainian]. URL: http://www.irbis-nbuv.gov.ua/cgi-bin/irbis\_nbuv/cgiirbis\_64.exe?I21DBN=LINK&P21DBN=UJRN&Z21ID=&S21REF=10&S21CNR=20&S21STN=1&S21FMT=ASP\_meta&C21COM=S&S2\_1S21P03=FILA=&S2\_1S21STR=KhU\_2015\_4\_3
3. Guriev SO, Kravtsov DI, Ordatsiy AV, Kazachkov VE., Goncharov OL, Bondar DV. [Clinical-nosological and clinical-anatomical characteristics of victims with mine injuries at the early hospital stage of medical care in modern hostilities on the example of the anti-terrorist operation in eastern Ukraine] // *Surgery of Ukraine*. 2016; 1: 7-11. [in Ukrainian]. URL: http://www.irbis-nbuv.gov.ua/cgi-bin/irbis\_nbuv/cgiirbis\_64.exe?I21DBN=LINK&P21DBN=UJRN&Z21ID=&S21REF=10&S21CNR=20&S21STN=1&S21FMT=ASP\_meta&C21COM=S&S2\_1S21P03=FILA=&S2\_1S21STR=Khhksh\_2016\_3\_25
4. Kutko II, Panchenko OA, Linyov OM. [Post-traumatic stress disorder in people who have endured armed conflict. Clinical diagnosis, treatment and rehabilitation] // *Ukrainian Medical Journal*. 2016; 1: 24-7. [in Russian]. URL: https://www.umj.com.ua/article/93343/posttravmaticheskoe-stressovoe-rasstrojstvo-u-perenesshix-vooruzhennyj-konflikt-klinicheskaya-dinamika-diagnostika-lechenie-i-reabilitaciya
5. Mishalov VG, Koval BM, Nagalyuk YV, Tsema EV, Rogovsky VM, Batyuk AI. [Gunshot wounds of the main vessels of the lower extremities. Key points of diagnosis and treatment] // *Heart and vessels*. 2017; 1: 91-104. [in Ukrainian]. URL: file:///C:/Users/%D0%A2%D0%B0%D1%82%D1%8C%D1%8F%D0%BD%D0%B0%20%D0%98%D0%B2%D0%B0%D0%BD%D0%BE%D0%B2%D0%BD%D0%B0/Downloads/sis\_2017\_1\_15.pdf
6. Radchenko OM. [Cardiac pathology associated with combat trauma: from the First World War to the present day] // *Therapia*. 2016; 6: 46-8. [in Ukrainian].
7. [Reaction to severe stress and maladaptation. Post-traumatic stress disorder (Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care)]. Order of the Ministry of Health of Ukraine 02/23/2016 // *NeuroNews: Psychoneurology and Neuropsychiatry*. 2016. 3(77): article 9. [in Ukrainian]. URL: https://neuronews.com.ua/ua/archive/2016/3%2877%29/article-1676/reakciya-na-vazhkiy-stres-ta-rozlad-adaptaciyi-posttravmatichniy-stresoviy-rozlad#gsc.tab=0
8. Ustinov O. [Military medical doctrine: a balanced response to the challenges of time] // *Ukrainian Medical Journal*. 2014;

- 5(103): 42-4. [in Ukrainian]. URL: <https://www.umj.com.ua/article/80976/vijskovo-medichna-doktrina-vivazhena-vidpovid-na-vikliki-chasu>
9. Fedorova O. Challenges of Ukrainian reality: features of emergency medical care in modern armed conflict (review) // Ukrainian Medical Journal. 2014. 5(103): 20-3. [in Russian]. URL: <https://www.umj.com.ua/article/80580/vyzovy-ukrainskoj-realnosti-osobennosti-okazaniya-ekstrennoj-medichskoj-pomoshhi-v-usloviyah-sovremennogo-vooruzhennogo-konflikta>
10. Tsybalyuk VI, Troyan OI, Komarnytsky VP Analysis of the results of surgical treatment of anti-terrorist operation participants in eastern Ukraine with gunshot wounds to the spinal cord and peripheral nerves with the use of electrical stimulation // Surgery of Ukraine. 2017; 3: 7-11. [in Ukrainian]. URL: [http://www.irbis-nbuv.gov.ua/cgi-bin/irbis\\_nbuv/cgiirbis\\_64.exe?I21DBN=LINK&P21DBN=UJRN&Z21ID=&S21REF=10&S21CNR=20&S21STN=1&S21FMT=ASP\\_meta&C21COM=S&2\\_S21P03=FILA=&2\\_S21STR=KhU\\_2017\\_3\\_3](http://www.irbis-nbuv.gov.ua/cgi-bin/irbis_nbuv/cgiirbis_64.exe?I21DBN=LINK&P21DBN=UJRN&Z21ID=&S21REF=10&S21CNR=20&S21STN=1&S21FMT=ASP_meta&C21COM=S&2_S21P03=FILA=&2_S21STR=KhU_2017_3_3)

## ДІАГНОСТИКА ТА ЛІКУВАННЯ БОЙОВИХ УШКОДЖЕНЬ СЕРЦЯ І МАГІСТРАЛЬНИХ СУДИН

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**Актуальність.** Відповідно до сучасних реалій бойових дій на Сході України, у медичній спільноті виріс запит на інформацію про характер найбільш небезпечних уражень учасників операції Об'єднаних сил (ООС) на Донбасі.

**Мета:** аналіз і узагальнення характеру травм серця, отриманих в умовах бойових дій на Сході України, етапів медичного супроводу таких поранених.

**Матеріали та методи.** Аналіз наукових публікацій в наукових фахових журналах України за ключовими словами за період 2014-2018рр.

**Результати.** Проаналізовано характер травм у учасників ООС. На 1 місці стоять поранення кровеносних судин з кровотечею (60%), на 2 – пневмоторакс (34%) і на 3 – порушення прохідності дихальних шляхів (6%). Все це може комбінуватись і доповнюватись ушкодженням нервової системи та інших органів. В умовах сучасної війни на Донбасі найчастішими видами травм вважають осколкові ураження (50,5%), кульові поранення (25,3%) та закриту травму (20,3%). Наведена класифікація травм серця, клінічна симптоматика, описані рівні супроводу такого пораненого: перша допомога на догоспітальному етапі («золота хвилина») на полі бою, кваліфікована допомога лікаря («золота година»), спеціалізована медична допомога в умовах лікарні. Описані посттравматичні стресові розлади, які тривають від одного до 6 місяців і потребують комплексного лікування.

**Висновки.** Згідно з новою військово-медичною доктриною НАТО, «ефективна і надійна система медичного забезпечення сприяє підтримці довіри військовослужбовців та широкої громадськості до армії та її політичного керівництва».

**Ключові слова:** бойова травма, поранення серця і судин, етапи медичного супроводу, лікування поранених.

## ДИАГНОСТИКА И ЛЕЧЕНИЕ БОЕВЫХ ПОВРЕЖДЕНИЙ СЕРДЦА И МАГИСТРАЛЬНЫХ СОСУДОВ

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**Актуальность.** Согласно современным реалиям боевых действий на Востоке Украины, в медицинском сообществе вырос запрос на информацию о характере наиболее опасных поражений участников операции Объединенных сил (ООС) в Донбассе.

**Цель:** анализ и обобщение характера травм сердца, полученных в условиях боевых действий на Востоке Украины, этапов медицинского сопровождения таких раненых.

**Материалы и методы.** Анализ научных публикаций в научных журналах Украины по ключевым словам за период 2014-2018 гг.

**Результаты.** Проанализирован характер травм у участников ООС. На 1 месте стоят ранения кровеносных сосудов с кровотечением (60%), на 2 – пневмоторакс (34%) и на 3 – нарушение проходимости дыхательных путей (6%). Все это может комбинироваться и дополняться повреждением нервной системы и других органов. В условиях современной войны на Донбассе частыми видами травм считают осколочные поражения (50,5%), пулевые ранения (25,3%) и закрытую травму (20,3%). Приведена классификация травм сердца, клиническая симптоматика, описаны уровни сопровождения такого раненого: первая помощь на догоспитальном этапе («золотые минуты») на поле боя, квалифицированная помощь врача («золотой час»), специализированная медицинская помощь в условиях больницы. Описаны посттравматические стрессовые расстройства, которые длятся от одного до 6 месяцев и требуют комплексного лечения.

**Вывод.** Согласно новой военно-медицинской доктрине НАТО, «эффективная и надежная система медицинского обеспечения способствует поддержке доверия военнослужащих и широкой общественности к армии и ее политическому руководству».

**Ключевые слова:** боевая травма, ранение сердца и сосудов, этапы медицинского сопровождения, лечение раненых

**ВІТАЄМО ПРОФЕСОРА ЗЯБЛІЦЕВА С.В. З 55-РІЧНИМ ЮБІЛЕЄМ!  
БАЖАЄМО УСПІХІВ У НАУКОВІЙ ТА ПЕДАГОГІЧНІЙ ДІЯЛЬНОСТІ,  
МІЦНОГО ЗДОРОВ'Я!**



### **ЗЯБЛІЦЕВ СЕРГІЙ ВОЛОДИМИРОВИЧ**

доктор медичних наук, професор кафедри патофізіології  
Національного медичного університету імені О. О. Богомольця,  
віце-президент Академії наук вищої освіти України з питань аналітичної,  
організаційно-методичної та організаційної діяльності

Зябліцев С.В. народився у липні 1965 р. Після закінчення в 1989 році лікувального факультету медичного інституту у Донецьку працював завідуючим відділом молекулярно-генетичних досліджень Центральної науково-дослідної лабораторії Донецького національного медичного університету ім. М. Горького. В 1992 році захистив кандидатську, а у 2005 році – докторську дисертацію. В 2007 році отримав вчене звання професора за фахом «патологічна фізіологія». З 2013 р. – завідувач кафедри патологічної фізіології Донецького національного медичного університету ім. М. Горького, а з 2014 року – професор кафедри патофізіології Національного медичного університету ім. О.О. Богомольця.

С.В. Зябліцев – висококваліфікований фахівець, провідний вчений в галузі патофізіології, представник однієї з найвидатніших наукових шкіл Донбасу – школи академіка Єльського В.М. Основні напрямки наукової діяльності – вивчення патофізіології нейроендокринної системи при травматичній хворобі, екстремальних станах, захворюваннях ендокринної системи. Під його керівництвом виконано 9 кандидатських дисертацій.

Завдяки високому професійному рівню С.В. Зябліцева, ще у 1994 році на базі Центральної науково-дослідної лабораторії Донецького медичного університету було створено одну з перших в Україні лабораторію молекулярно-генетичного аналізу і впроваджено ідентифікацію геному людини. Зябліцев С.В. є експертом з питань встановлення особистості у судово-медичній практиці. Пріоритетним напрямком є оцінка значення молекулярно-генетичних порушень у розвитку найбільш поширених захворювань (серцево-судинних, онкологічних репродуктивних та нейро-ендокринних). Під керівництвом С.В. Зябліцева з 2006 року було розроблено і впроваджено в медичну практику лабораторну інформаційну систему «УРАН», застосування якої дозволило суттєво підвищити рівень якості лабораторної інформації, необхідної для діагностики, контролю за лікуванням, профілактики захворювань.

С.В. Зябліцев – член спеціалізованої вченої ради при НДІ Фізіології імені О.О. Богомольця, член редакційних колегій низки медичних часописів. Автор більш 500 наукових робіт, в тому числі 12 монографій, основні з них: «Синдроми травматичної хвороби при черепно-мозковій травмі» (2020), «Ендотеліальна дисфункція при гломерулонефриті» (2006 р.), «Нейрогормональні регуляторні механізми при черепно-мозковій травмі» (2008 р.), «Моделювання черепно-мозковій травми» (2008 р.), «Синдроми атопічної хвороби» (2008 р.), «Гормонодіагностика патології репродуктивної функції» (2010 р.), «Запалення шкіри» (2011 р.), «Патогенетична корекція нанопрепаратом ліпосом ліпідної пероксидації при синдромі тривалого роздавлювання» (2012 р.), «Флаґман освіти і науки України», «Флаґман сучасної медицини» (2014) та грамотами «За вагомий внесок у розвиток освіти і науки України» МОН України (2013 р.) та «За охорону здоров'я нації» Комітету Верховної Ради України з питань охорони здоров'я і НАМН України (2014 р.).

Видатні наукові досягнення С.В. Зябліцева оцінено науковою громадою України – з 2008 року він обраний академіком Національної академії наук вищої освіти України. За самовіддану та плідну наукову, педагогічну та організаційну працю С.В. Зябліцева відзначено медалями Академії «За успіхи в науково-педагогічній діяльності» (2010 р.), Почесною медаллю «20 років АНВОУ» (2012 р.), Ярослава Мудрого (2013) та Святого Володимира (2019), «Флаґман освіти і науки України», «Флаґман сучасної медицини» (2014) та грамотами «За вагомий внесок у розвиток освіти і науки України» МОН України (2013 р.) та «За охорону здоров'я нації» Комітету Верховної Ради України з питань охорони здоров'я і НАМН України (2014 р.).

**Колеги, друзі**

