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INFLUENCE OF KETOSIS AND GLYCEMIA LEVELS ON CRAVING FOR ETHANOL IN ALCOHOLIZED RATS

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Relevance. In case of developed alcoholic disease, under conditions of alcoholic hypoglycemia, ketone bodies act as an energy substrate for the brain. However, the role of ketone hunger for maintaining the craving for alcohol has not been established. The assumption of such a connection has a right to exist, since it is alcohol that stimulates the formation of ketone bodies. Therefore, with developed alcoholism, the desire to consume alcohol (and, in fact, "saturate" the brain with ketone bodies) can be considered as a consequence of hypoketonemia. Accordingly, the hunger of the alcoholic is the result of hypoketonemia, but not hypoglycemia. Therefore, it is relevant to conduct a study in which the given variables (controlled by us) were the level of glycemia and the level of ketonemia, and the amount of alcohol consumed voluntarily (under conditions of free choice) was a derivative and dependent value.

Objective: to study the relationship between craving for alcohol, and levels of glycemia and ketonemia in alcoholized rats.

Materials and methods. Male white rats (n = 40) were forcibly alcoholized with 10% ethanol in 16 weeks. After that, for 30 days, they had a free choice of three types of drinking: clean water, 5% glucose, and 10% ethanol. The volume of consumed liquids was recorded. The criterion for the developed alcohol dependence was the preference of ethanol. At this stage, the animals were divided into 4 groups. Rats were injected per os with 0.8-1.5 ml of: 1.4% unitiol (3.5 mg / kg) to suppress ketonemia – group 1 (n = 10); 40% starch (1.0 g / kg) to eliminate hypoglycemia – group 2 (n = 10); 2.8% unitiol and 80% starch to suppress ketonemia and eliminate hypoglycemia – group 3 (n = 10); 0.9% NaCl as a control – group 4 (n = 10). Blood glucose (from the tail vein) and urine ketone bodies were monitored. The glucose level was determined with a glucometer. Test strips were used to detect ketone bodies in urine. The results were processed with *MedStat* software. To measure the strength of the correlation between the indicators, Spearman and Pearson tests were used.

Results. No ketone bodies were found in the urine of healthy animals; however, after the end of forced alcoholization, varying levels of ketonuria were recorded in all rats: from 0.5 to 10 mmol / L (Spearman's rank correlation test was 0.8). Glycemia in healthy rats was 7.0 ± 1.4 mmol / L. After alcoholization, it decreased ($p < 0.001$) to 3.0 ± 0.7 mmol / l. Ethanol consumption during first 10 days of forced alcoholization was 3.2 ± 0.7 ml per 100 g of animal weight; by the end of the third week - 4.9 ± 1.1 ml; by the end of the sixth week - 6.4 ± 1.4 ml (this was a climax of consumption, since consumption did not increase up to the 16th week).

After a 30-day correction, the level of glycemia (mmol / L) was as follows: animals of the 1st group (unitiol) - 4.0 ± 0.8; animals of the 2nd group (enhanced carbohydrate diet) - 7.1 ± 1.2; animals of the 3rd group (unitiol + enhanced carbohydrate diet) - 7.1 ± 1.1; animals of the 4th group (0.9% NaCl) - 3.5 ± 0.8.

Alcohol consumption (ml per 100 g of animal weight) after 30-day correction was as follows: in group 1 (unitiol) - 5.1 ± 0.9; in group 2 (enhanced carbohydrate diet) - 2.7 ± 1; in group 3 (unitiol + enhanced carbohydrate diet) - 3.5 ± 1.5; in group 4 (0.9% NaCl) - 4.5 ± 1.2.

A positive strong correlation was found between ethanol consumption and a decrease in glycemia (Pearson's test – 0.8).

Conclusion. In alcoholized animals with severe hypoglycemia and ketosis, drug suppression of ketosis does not reduce the craving for ethanol. Metabolic correction, aimed at eliminating hypoglycemia, helps to reduce alcohol consumption and reduce the severity of ketosis. The reason for maintaining a stable craving for alcohol is the metabolic demand of the brain for ketone bodies, as alternative food sources in conditions of alcoholic hypoglycemia, and the synthesis of which is stimulated by alcohol intake.

Key words: alcohol addiction, hypoglycemia, ketosis, metabolic correction, rats.

Relevance. The relevance of this study was defined by the widespread prevalence of alcoholism [1]. Alcoholism has acquired such a scale that it threatens the degeneration of the nation. Despite certain achievements of modern medicine in the fight against this disease, the percentage of relapses is still very high: according to various estimates, it reaches 60-90% of cases. According to the testimony of the patients themselves, the most difficult thing is to overcome the craving for alcohol [2]. This study is devoted to the problem of the etiology of attraction to alcohol.

Earlier, we conducted a series of experiments [3], the results of which allowed us to formulate a working hypothesis explaining the cause of the pathological craving for alcohol. It is known that in the causal relationship of the pathogenesis of alcoholism, ethanol is the cause, and hypoglycemia and ketosis are the consequences. Due to long-term hypoglycemia, the cells of an alcoholized organism undergo deep reorganization of enzymatic systems and switch to nutrition by ketone bodies, which become the main “fuel” molecules [4, 5]. The formation of ketone bodies is stimulated by ethanol.

We hypothesize the following: just as a healthy body depends on glucose, the main nutrient substrate, so an alcoholized body depends on ketone bodies, the main energy substrate in hypoglycemia. In a healthy

body, with a decrease in glucose concentration in the blood, a feeling of hunger arises, and in an alcoholized body, with a decrease in ketone bodies level in the blood, a kind of hunger arises too. But, since the formation of ketone bodies is stimulated by large doses of ethanol, the distinctive feature of alcoholic hunger is the attraction not to traditional food (as a supplier of glucose), but to ethanol (as a supplier of ketone bodies).

As a result, at a certain stage of alcoholism, the appearance of the desire to drink alcohol can be considered as a consequence of hypoketonemia.

In this study, to test this hypothesis, we used a model of experiment in which the specified variables (controlled by us) were the levels of glycemia and ketonemia; and the volume of alcohol consumed voluntarily, under conditions of free choice, was the derivative and dependent value. At the same time, we proceeded from the general physiological principle that attraction to anything, as a behavioral reaction, is a reflection of the internal needs of the organism.

Objective: to study the relationship between craving for alcohol and levels of glycemia and ketonemia in alcoholized rats.

MATERIALS AND METHODS

The experiment was carried out on 40 rats of both sexes, 12-15 months old, weighing 200-350 g in the autumn-winter period at the vivarium with forced ventilation. The study followed the requirements of the "European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes". The temperature in the vivarium was maintained at the level of 17-22 ºC, which excluded excessive thirst. The food was balanced, that also allowed the drinking behavior to be maintained at a constant level. The animals were kept separately, one rat per cage, with free access to food.

Access to drinking was not always the same. First, for one week, two drinkers were placed into each cage: with clean water, and 5% glucose, i.e. the rats had a free choice of drinking. The amount consumed liquid from each drinker was recorded. In this way, the hedonic properties of glucose were determined for each animal. Then, for 16 weeks, forced alcoholization was carried out: in each cage, there was only one drinker with 10% ethanol.

After the end of forced alcoholization, the animals had a free choice between three types of liquids for 30 days: clean water, 5% glucose, and 10% ethanol. The criterion for the developed alcohol addiction was the preference of ethanol. Since the animals significantly differed in weight, the volume of liquid they drunk (ml) was calculated per 100 g of body weight.

At this stage, the animals were divided into three groups. Rats of group 1 (n = 10), in order to eliminate ketosis, were injected with 1.4% solution of unithiol (3.5 mg / kg) for 30 days, 3 times a day with an interval of 5 hours, *per os* from a syringe without a needle. The volume of administration ranged from 0.8 ml to 1.5 ml, depending on the weight of the animal. Rats of group 2 (n = 10), in order to eliminate hypoglycemia, were injected with the same amount of boiled jelly with 40% starch (1.0 g / kg in terms of glucose). The choice of starch is defined by the fact that this complex polysaccharide with a branched chain is being broken down for a long time in the gastrointestinal tract of the rat. Released glucose is absorbed gradually, which ensures the maintenance of a stable level of glucose in the blood for a long time and does not provoke an overstrain of pancreatic insular apparatus.

Animals of group 3 (n = 10), in order to eliminate ketosis and hypoglycemia, were injected with a 2.8% solution of unithiol and jelly with 80% starch. In order not to increase the total volume of administration, the concentrations of unithiol (up to 2.8%) and starch (up to 80%) were increased. Rats of group 4 (controls, n = 10) were injected with 1.0 ml of 0.9% sodium chloride.

Throughout the experiment, blood glucose level and urine ketone bodies were monitored:

- before the start of the experiment,
- at the end of forced alcoholization (16th week of the experiment),
- one, two and three decades after the end of alcoholization, in conditions of free choice of drinking, with the background of oral administration of one of the mentioned above substances.

The sampling of biological fluids was carried out in the morning, before the oral administration of the substances. The animals were fasting: the feeding trough was removed from the cage the night before. A drop of blood was taken from the tail vein. Urine was collected by placing the rat in a plastic container with a perforated bottom. The urine drained into the pan.

Blood glucose level was determined with a glucometer and test strips (Longevita, UK). The sensitivity of the method is 0.1 mmol / L. A preliminary calibration study was carried out, determining the glucose level in the same blood samples (n = 20) with a glucometer and glucose oxidation method using standard kits (Lachema). There were no discrepancies in the results, with an accuracy of 0.1 mmol / L.

To identify ketone bodies in urine, *Citolab* test strips (Farmasco, Ukraine) were used. Sodium nitroprusside was applied to the paper of the test strips,

upon interaction with which ketone bodies give a red-violet coloration. The intensity of the color varies with the concentration of ketone bodies. To evaluate the results, a scale suggested by the manufacturer was used:

"-" - no ketones;

"±" - concentration of ketones up to 5 mg / dl (up to 0.5 mmol / L);

"+" - concentration of ketones 6-15 mg / dl (0.6-1.5 mmol / L);

"++" - the concentration of ketones is 16-40 mg / dl (1.6-4.0 mmol / L);

"+++" - the concentration of ketones is 41-100 mg / dl (4.1-10 mmol / L).

The experimental results were assessed with *MedStat* software.

Since the distribution of the values of the volume of the consumed solution of glucose and alcohol did not differ from normal, parametric criteria were used. To represent these data, the average value of the volume of consumed liquid X (ml / 100 g) and the standard deviation s (ml / 100 g) were used.

The qualitative indicators of urine ketone levels were assigned categories from 0 to 5. To present these data, the frequency of occurrence of the corresponding level of ketonuria (%) and the standard error m (%) were used. Since the distribution differed from the normal one ($p < 0.05$), nonparametric comparison criteria were used for the analysis: comparison of centers of related samples using a two-sided test, Wilcoxon's T-test, Kruskal-Wallis rank one-way ANOVA; in cases of statistically significant differences between the groups, pairwise comparison was carried out with Dunn's test.

In the course of the analysis, multiple comparisons were made to determine the differences in the means in the unrelated groups for quantitative characteristics that correspond to a normal distribution (ethanol consumption and blood glucose levels); the means for each group in different periods of the experiment were also compared.

To measure the strength of the correlation between the indicators, Spearman and Pearson rank correlation tests were used.

RESULTS AND DISCUSSION

For convenience, the results obtained at each stage of the experiment are considered separately.

Stage I: before the start of the experiment, healthy rats.

No ketone bodies were found in the urine of healthy animals before forced alcoholization (Table 1).

The blood glucose level in the tail vein of healthy rats was 7.0 ± 1.4 mmol / L, the reference interval was 6.6-7.4 mmol / L, i.e. the value of this constant in rats is higher than in humans (3.3-5.5 mmol / l).

Stage II: forced alcoholization.

The consumption of ethanol during forced alcoholization is shown in Figure 1. The consumption of ethanol during forced alcoholization was as follows. In the first 4-10 days, the animals drank ethanol at an average rate of 3.2 ± 0.7 ml / 100 g of body weight. By the end of the third week, the amount of consumed ethanol increased to an average of 4.9 ± 1.1 ml / 100 g of body weight. By the end of the sixth week, there was another peak in the consumption of ethanol – up to 6.4 ± 1.4 ml / 100 g of animal weight. When comparing the average indicators of the drinking regime in the periods from 4 to 10 days, and at the third week, a statistically significant ($p < 0.001$) increase in the amount of consumed ethanol was found. When comparing similar averages at 3 and 6 weeks, a statisti-

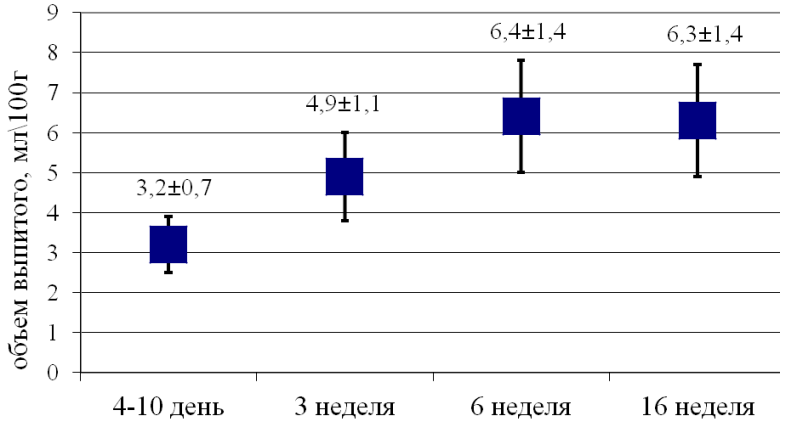

Fig. 1. Levels of alcohol consumption by rats in different periods of forced alcoholization. On the horizontal axis: periods of forced alcoholization – 4-10 days, third week, sixth week, sixteenth week. On the vertical axis: volume of consumed 10% ethanol per 100 g of animal weight (ml / 100 g), ± *s*

cally significant (p <0.001) increase in the drinking regimen was also found. Thus, there is an increase in the volume of alcohol consumed from one reporting period to another.

At the same time, during the experiment, it was noted that alcohol consumption at the sixth week was a climax of consumption, since later, despite the ongoing forced alcoholization, this amount remained approximately constant for each individual, with slight fluctuations. The stability of ethanol consumption from the sixth to the sixteenth week indicates the developed alcohol addiction (the change in indicators compared to the sixth week is not statistically significant, p = 0.82).

A comparison of blood glucose levels before and after alcoholization was made. A statistically significant decrease in the level of glycemia (p <0.001) was established from 7.0 ± 1.4 mmol / L to 3.0 ± 0.7 mmol / L. When conducting a correlation analysis of the level of ethanol consumption at the end of forced alcoholization, and the degree of decrease in blood glucose levels during this period, a positive strong relationship was revealed between these indicators (Pearson's correlation test – 0.8). In addition, in all rats, without exception, after the end of forced alcoholization, ketonuria of varying severity was recorded (Figure 2).

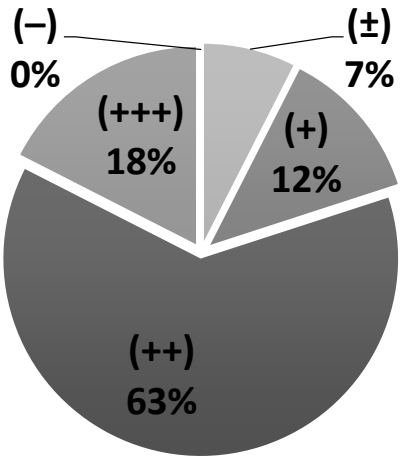

Fig. 2. The severity of ketonuria in rats after the end of forced alcoholization

Stage III: abolition of forced alcoholization, conditions for free choice of drinking.

After the end of forced alcoholization, under conditions of free choice, the rats were observed for another three weeks. The effect of forced administration of the preparation of unitiol and starch on the level of ketonuria in the study groups during this period of the experiment can be seen in Figures 3-6.

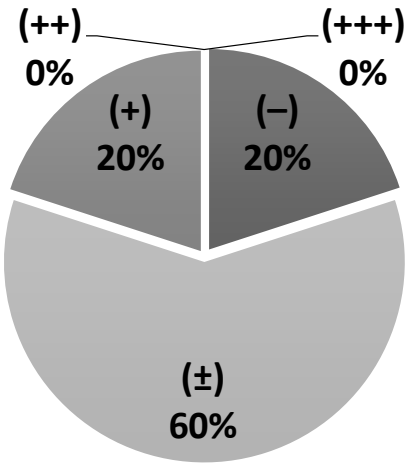

Fig. 3. The severity of ketonuria in alcoholized rats of group 1, received metabolic correction with the drug unithiol for 30 days

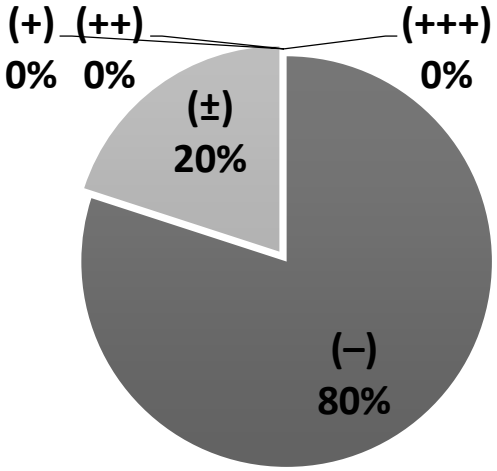

Fig. 4. The severity of ketonuria in alcoholized rats of group 2, received metabolic correction for 30 days with boiled jelly of 40% starch

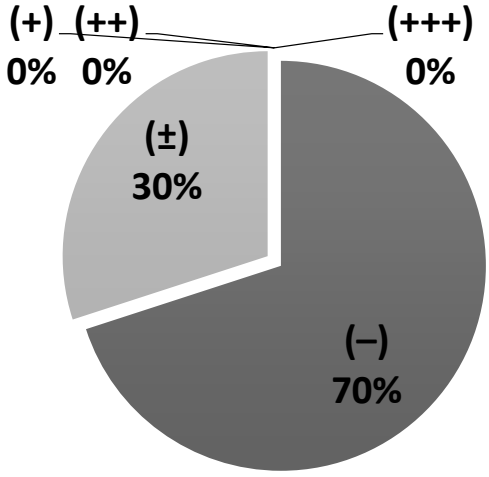

Fig. 5. The severity of ketonuria in alcoholized rats of group 3, received combined metabolic correction with unithiol and starch for 30 days

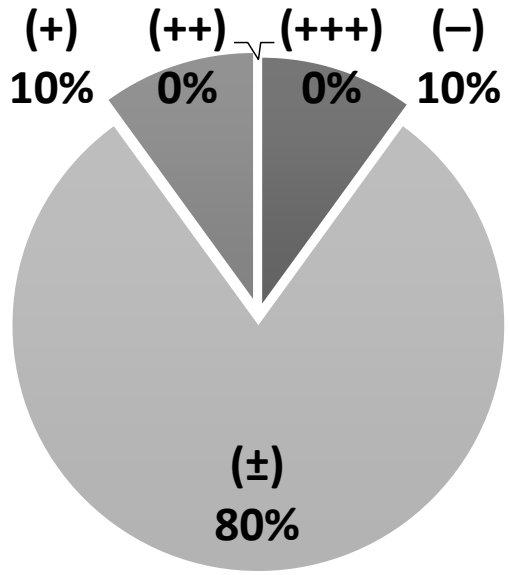

Fig. 6. The severity of ketonuria in alcoholized rats of group 4 (controls), that did not receive metabolic correction for 30 days

The influence of the studied variants of metabolic correction on the levels of ethanol consumption and glycemia is shown in Table 1.

Table 1

Influence of forced administration of unithiol and starch solutions on blood glucose and on the volume of ethanol consumed by rats at different times after the end of forced alcoholization, under conditions of free choice

Group	Substance, used *per os*	Duration of administration *per os*, decades	Consumption of 10% ethanol, $X \pm s$, ml per 100 g of weight	Blood glucose level, $X \pm s$, mmol/L
1, n = 10	Unithiol	One	5,1±1,2	3,6±0,8
		Two	4,3±0,8	3,8±0,9
		Three	5,1±0,9	4,0±0,8
2, n = 10	Starch	One	4,5±1,1	6,0±1,4
		Two	3,2±1,2	6,1±1,8
		Three	2,7±1	7,1±1,2
3, n = 10	Unithiol + starch	One	5,2±1,1	6,0±1,2
		Two	3,1±1,3	6,0±1,4
		Three	3,5±1,5	7,1±1,1
4, n = 10	Sodium chloride	One	5,5±0,9	3,0±0,7
		Two	4,5±1	3,2±0,7
		Three	4,5±1,2	3,5±0,8

Analysis of the presented data allows us to draw a number of conclusions:

- the consumption of large amounts of ethanol is accompanied by pronounced ketosis (Spearman rank correlation test – 0.8), and a significant decrease in the level of glycemia (Pearson correlation test – 0.8);

- an artificial elimination of ketosis with unithiol (group 1) has a short-term effect; ketosis resumes and persists as long as the animals consume a large amount of alcohol (there were no statistically significant differences between the studied parameters after the first and third decades of treatment);

- systematic administration of unithiol (group 1) leads to a statistically significant decrease ($p < 0.001$) in the manifestation of ketosis compared with the controls (group 40;

- an artificial suppression of ketosis with unithiol (group 1) does not reduce the craving for ethanol and does not contribute to a decrease in hypoglycemia (no statistically significant differences were found between these indicators when comparing their values at 16 weeks of forced alcoholization and after the third decade of unithiol administration);

- the elimination of ketosis is largely promoted not by the administration of unithiol (group 1), but by the elimination of hypoglycemia (groups 2 and 3), which can be seen from the indicators of the degrees of ketonuria;

- elimination of hypoglycemia contributes not only to the elimination of ketosis, but also to a decrease in the craving for ethanol (in groups 2 and 3, the level of ketonuria decreased to the level of healthy rats after the first decade of treatment, and remained the same during the second and third decades; no statistically significant differences were found between these indicators before the onset of alcoholism and after 1-3 decades of treatment; the level of ethanol consumption in these groups significantly decreased from the first to the second, and from the second to the third decade of treatment, $p < 0.001$);

- the weakening of addiction to ethanol occurs not due to the elimination of ketosis (group 1), but due to the elimination of hypoglycemia (groups 2 and 3);

- long-term (during 30 days) forced starch feeding (groups 2 and 3) contributes to the normalization of blood glucose levels (the level of glycemia in rats in these groups significantly increased to the level of healthy rats after the first decade of treatment and remained so during the second and the third decade of treatment);

- in alcohol-dependent rats, under conditions of free choice (group 4), a high level of alcohol consumption, ketosis, hypoglycemia remains (when comparing glycemic indicators at 16 weeks of forced alco-

holization and after 30 days under conditions of free choice, the differences were not statistically significant ($p = 0.088$), and the rate of ketonuria, although it decreased, did not reach the level of healthy rats ($p = 0.004$).

Analyzing the results of this work, we can assume that a metabolic correction that would restore the sensitivity of brain cells to glucose, would contribute to an increase in glucose utilization by the brain, could contribute to a decrease in alcohol addiction. Obviously, this is possible when the proper activity of glycolysis enzymes is restored. This would help the brain to utilize ketones to a lesser extent as a nutrient substrate, and in the long term, it would make it easier to quit alcohol. To do this, it is necessary to eliminate hypoglycemia. According to our data, it is very important that this correction is not brief.

In our opinion, the fact that long-term administration of unithiol to rats did not reduce alcohol consumption suggests that artificial elimination of ketosis, depriving the brain of a nutrient substrate, only provokes the body to consume alcohol, which is a powerful stimulator of ketone bodies formation. The positive effect of its administration in acute conditions is due only to the elimination of acidosis and the toxic effect of ketones on the brain, and, as a consequence, the elimination of unpleasant subjective sensations (nausea, vomiting, unpleasant smell of fumes). Another confirmation of this conclusion is that, despite the prolonged administration of a solution of unithiol, the concentration of ketone bodies in urine (and therefore in the blood) did not decrease, remaining, although not at a high, but stable level (up to 0.5 mmol / L). The explanation of the presence of ketone bodies in urine, despite the administration of unithiol, may partly follow from the pharmacodynamics of the drug. The half-life of unithiol is 7.5 ± 0.46 hours. The time spent in the blood is 9-11 hours. Since about 15 hours elapsed between the last administration of unithiol (at 5 p.m.) and its determination in urine (at 8 a.m.), the concentration of ketone bodies probably had time to increase.

Therefore, according to our results, the factors that keep the craving for alcohol for a long time are hypoglycemia and the need for ketone bodies. Therefore, we propose a new approach to suppressing the craving for alcohol, the essence of which is a long-term metabolic correction with carbohydrates, which stimulates the restoration of the initial activity of the enzyme systems of brain cells and a return to glucose nutrition. Despite its apparent simplicity, this approach can be quite effective. Due to its simplicity and accessibility, it can constitute an alternative to the existing modern domestic practice of treating addictive disorders, which, according to experts, differs significantly from the world therapeutic approaches by the inadequate variety of drugs used, the unjustified use of psychotropic drugs and the lack of sufficient scientific substantiation of the accepted methods of treatment [6].

CONCLUSIONS

In alcoholized animals with severe hypoglycemia and ketosis, drug suppression of ketosis does not reduce the craving for ethanol. Metabolic correction, aimed at eliminating hypoglycemia, helps to reduce alcohol consumption and reduce the severity of ketosis. The reason for maintaining a stable craving for alcohol is the metabolic demand of the brain for ketone bodies, as alternative food sources in conditions of alcoholic hypoglycemia, and the synthesis of which is stimulated by alcohol intake.

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ВПЛИВ РІВНЯ КЕТОЗУ ТА ГЛІКЕМІЇ НА ПОТЯГ ДО ЕТАНОЛУ У АЛКОГОЛІЗОВАНИХ ЩУРІВ

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Актуальність. При сформованій алкогольній хворобі в умовах алкогольної гіпоглікемії енергетичним субстратом для мозку виступають кетонові тіла. Але досі не вирішено питання значення кетонового голоду для підтримки потягу до алкоголю. Припущення про наявність такого зв'язку має право існування, оскільки саме алкоголь стимулює утворення кетонових тіл. Тому при алкоголізмі, що сформувався, бажання вжити алкоголь (а фактично «наситити» мозок кетоновими тілами) можна розглядати вже як наслідок гіпокетонемії. Відповідно, голод алкоголіка – це результат гіпокетонемії, але не гіпоглікемії. Тому актуальним є дослідження, в якому заданими змінними (керованими і контрольованими нами) були рівень глікемії та рівень кетонемії, а похідною і залежною від них величиною була кількість добровільно випитого алкоголю, в умовах вільного вибору.

Ціль: вивчити взаємозв'язок потягу до алкоголю та рівнів глікемії та кетонемії у алкоголізованих щурів.

Матеріали та методи. Самців білих щурів (n=40) протягом 16 тижнів примусово алкоголізували 10 % етанолом. Після цього протягом 30 днів був вільний вибір між трьома видами пиття: водою, 5 % глюкозою, 10 % етанолом. Реєстрували кількість випитого. Критерієм сформованої алкогольної залежності була перевага етанолу. На цьому етапі тварини розділили на 4 групи. Щурам *per os* вводили 0,8-1,5 мл певної речовини: 1 група (n=10), для придушення кетонемії – 1,4 % унітіол (3,5 мг/кг); 2 група (n=10), для усунення гіпоглікемії – 40 % крохмаль (1,0 г/кг); 3 група (n=10), для придушення кетонемії та усунення гіпоглікемії – 2,8 % унітіол та 80 % крохмаль; 4 група (n=10), контрольна – 0,9 % NaCl. Проводили моніторинг вмісту глюкози в крові (з хвостової вени) та кетонових тіл у сечі. Рівень глюкози визначали за допомогою глюкометра. Для виявлення кетонових тіл у сечі використовували тест-смужки. Під час обробки результатів використовували пакет MedStat. Для вимірювання сили кореляційного зв'язку між показниками використовували показники рангової кореляції Спірмена та Пірсона.

Результати. Кетонових тіл у сечі здорових тварин не виявлено. Проте після закінчення примусової алкоголізації в усіх щурів реєструвалася кетонурія різного ступеня вираженості: від 0,5 до 10 ммоль/л (показник рангової кореляції Спірмена - 0,8). Глікемія у здорових щурів 7,0±1,4 ммоль/л; під час алкоголізації вона знизилася ($p<0,001$) до 3,0±0,7 ммоль/л. Споживання етанолу (мл на 100 г ваги тварини) під час примусової алкоголізації: перші 10 днів – 3,2±0,7; до кінця третього тижня – 49 ± 11; до кінця шостого тижня – 6,4±1,4 (це «стеля» споживання, тому що далі, до 16 тижня споживання алкоголю не збільшувалося).

Після 30-денної корекції рівень глікемії (ммоль/л) був таким: тварини 1-ї групи (унітіол) – 4,0±0,8; тварини 2-ї групи (посилена вуглеводна дієта) – 7,1±1,2; тварини 3-ї групи (унітіол+ посилена вуглеводна дієта) – 7,1±1,1; тварини 4-ї групи (0,9 % NaCl) – 3,5±0,8.Споживання алкоголю (мл на 100г ваги тварини) після 30-денної корекції таке: у 1-й групі (унітіол) – 5,1±0,9; у 2-й групі (посилена вуглеводна дієта) – 2,7±1; у 3-й групі (унітіол+ посилена вуглеводна дієта) – 3,5±1,5; у 4-й групі (0,9 % NaCl) – 4,5±1,2.

Виявлено позитивний сильний зв'язок (коефіцієнт кореляції Пірсона - 0,8) між споживанням етанолу та зниженням глікемії.

Висновок. У алкоголізованих тварин з вираженою гіпоглікемією та кетозом лікарське пригнічення кетозу не зменшує потягу до етанолу. Метаболічна корекція, спрямована на усунення гіпоглікемії, сприяє зниженню споживання алкоголю та зменшенню вираженості кетозу. Причиною утримання стійкого потягу до алкоголю є метаболічна потреба мозку в кетонових тілах як альтернативних джерелах харчування в умовах алкогольної гіпоглікемії, і синтез яких стимулюється прийомом алкоголю.

Ключові слова: алкогольна залежність, гіпоглікемія, кетоз, метаболічна корекція, щури.