



ETHOLOGICAL STUDY OF THE STATE OF ANXIETY IN RATS WITH CHRONIC NICKEL NITRATE POISONING ON THE BACKGROUND OF EXPERIMENTAL ATHEROSCLEROSIS

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Access this article online:	Abstract:
<p>QR code:</p> 	<p>The purpose of this study was to study the effect of chronic poisoning with nickel nitrate in experimental atherosclerosis on the state of anxiety in the «elevated plus maze» test. The experiments were carried out on 50 white non-linear male rats. The model of atherosclerosis was created according to I.V. Savitsky et al. (2016), which is based on the polyetiological theory of the development of the disease. After modeling atherosclerosis, poisoning with nickel nitrate was carried out through the drinking water for 60 days at a dose of 2 mg/kg.</p> <p>The results showed that the behavioral disturbances that occurred after the modeling of atherosclerosis were aggravated after poisoning with nickel nitrate. In particular, in the «elevated plus maze» test, adequate parameters visually reflecting the state of anxiety were manifested in active avoidance of the open space of the maze, in a decrease in the number of vertical stands, in a decrease in the number of hanging from open sleeves, in a decrease in the number of looks from closed sleeves, as well as in a decrease of grooming number with a corresponding increase in its duration. Maximum disturbances were observed two months after exposure to nickel nitrate. The obtained data show a toxic neurotropic effect of chronic intoxication with nickel nitrate in experimental atherosclerosis and highlight the necessity of creating efficient remediation methods.</p>
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INTRODUCTION

Pollution with heavy metals is one of the most harmful factors, having a wide range of dangerous consequences both for human health and for the lives of organisms. High concentrations of heavy metals caused by technogenic processes, as a result of

bioaccumulation, are currently found in all-natural environments. Over time, heavy metals enter the human body through the food chain [14, 15] and lead to an increase in cardiovascular, cancer, occupational, and other diseases [1, 2, 3, 4, 8, 9, 10].

Moreover, an analysis of recent scientific literature shows that exposure to heavy metals is

an important and underestimated risk factor related to the development of atherosclerosis and its consequences [5, 6, 7]. Researchers have put forward the hypothesis that heavy metals may be markers of the risk of developing atherosclerosis [11, 15].

Considering that atherosclerotic lesions at the level of the cardiovascular system are the main cause of people's mortality, the purpose of this study was to study the effect of chronic poisoning with nickel nitrate on the course of experimental atherosclerosis.

MATERIALS AND METHODS

The experiments were carried out on 150 white non-linear male rats. For experimental studies, the model of atherosclerosis according to I.V. Savitsky et al. [16], which is based on the polyetiological theory of disease development, was chosen. The animals received Mercazolil (25 mg/kg body weight), methylprednisolone (0.17 mg/kg body weight), and a 15% aqueous solution of ethyl alcohol in free access instead of water against the background of an atherogenic diet for 2 weeks. After 2 weeks, the level of total cholesterol, high-density lipoproteins, and low-density lipoproteins were studied in the rat blood serum for confirmation of atherosclerotic changes.

After modeling atherosclerosis, animals were exposed to chronic nickel nitrate. Poisoning with nickel nitrate was carried out through drinking water for 60 days at a dose of 2 mg/kg. The mother liquor of heavy metals was prepared by the calculation using the equation $A=(X \cdot B) \cdot C$, where X-factor = 6.77, B is the average weight of the rat, and C is the average daily water consumption of animals.

The elevated plus maze test is one of the most important and widely used tests for assessing nervous system function. It has been used for decades to assess the effects of chemical and physical agents and is considered one of the most sensitive models for the study of animal anxiety [12, 13].

The studies were carried out using the standard "elevated plus maze" setup before and after modeling atherosclerosis, and respectively 15, 30, and 60 days after poisoning against the

background of experimental atherosclerosis. The testing time was 5 minutes, during which the following parameters were recorded: the time spent in open sleeves, the number of looks from the closed sleeves, the number of vertical stands hanging from open sleeves, as well as the number of grooming reactions and their duration.

The experiments were carried out on laboratory animals, considering the standards of storage, care, and feeding approved by the principles of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes" (Strasbourg, 1986). The digital results of the study were processed statistically using the Student's t-test, and the reliability of the results was accepted at a difference of $p < 0.05$.

RESULTS AND DISCUSSION

The results of studies of behavioral reactions in the "elevated plus maze" test showed the following changes (Table 1).

After modeling atherosclerosis, the time spent in open sleeves changed slightly compared to data from intact animals. However, the number of hanging from open sleeves decreased by an average of 21% ($p < 0.01$), the number of looks from closed sleeves also decreased (by 9%), and the number of vertical stands in closed sleeves decreased by an average of 7% compared to corresponding data from intact rats. The number of grooming reactions after modeling atherosclerosis increased significantly (by an average of 43%), but the duration of grooming did not change compared to the data from intact animals.

Chronic poisoning of animals with nickel nitrate after modeling atherosclerosis led to pronounced changes in the behavioral reactions of the tested rats. Thus, the time spent in open sleeves began to decrease progressively: by 23% ($p < 0.001$) after 15 days, by 34% ($p < 0.001$) after a month, and by 47% ($p < 0.001$) after a two-month poisoning, respectively. The number of hangings from open sleeves, which was reduced after modeling atherosclerosis, continued to decrease even more, and on days 30 and 60 of poisoning, it was reduced by 42% ($p < 0.001$) and

52% ($p < 0.001$), respectively, in comparison with data from intact animals.

The number of looks from closed sleeves and the number of stands in closed sleeves also progressively decreased after the start of the poisoning. Thus, the number of looks from closed sleeves after 15 days decreased by 11% ($p < 0.05$), after 30 days by an average of 27% ($p < 0.01$), and 60 days after poisoning by an average of 47% ($p < 0.001$), respectively, with data from intact animals. The number of vertical stands decreased by 11% after 15 days, by 51%

($p < 0.001$), and by 63% ($p < 0.001$), respectively, after 30 and 60 days from the start of exposure. However, 15 days after the start of poisoning, the number of grooming reactions, compared to intact animals, was 18% greater, while with an increase in the poisoning period, the number of grooming reactions decreased on the 30th and 60th days by 11% and 26% ($p < 0.01$), respectively. Along with this, the duration of grooming also increased, and on the 30th and 60th days from the start, it averaged 40% ($p < 0.01$) and 64% ($p < 0.001$), respectively.

Table 1. Behavioral reactions of rats in the «elevated plus maze» test after poisoning with nickel nitrate against the background of experimental atherosclerosis ($M \pm m$, $n = 10$)

Indicators	Intact state	After modeling atherosclerosis	After poisoning		
			15 days	30 days	2 months
Time spent in open-sleeves	106.7 ± 16.5	111.4 ± 16.1	82.9 ± 13.3 ***	67.9 ± 9.26 ***	55.9 ± 9.3 ***
Number of hangs from open sleeves	6.2 ± 1.03	4.9 ± 0.74 **	4.9 ± 0.99 **	3.6 ± 0.84 ***	2.6 ± 0.7 ***
Number of looks from closed sleeves	8 ± 1.16	7.3 ± 1.25	7.1 ± 0.99 *	5.8 ± 1.23 **	4.2 ± 1.23 ***
Vertical stands in closed sleeves	9.7 ± 1.64	9 ± 1.25	8.6 ± 0.97	4.7 ± 1.16 ***	3.6 ± 1.08 ***
Number of grooming reactions	3.9 ± 0.99	5.6 ± 1.43 **	4.6 ± 1.84	3.5 ± 0.97	2.9 ± 0.88 *
Duration of grooming	11 ± 1.563	11 ± 0.94	11.7 ± 1.7	15.4 ± 2.59 **	18 ± 1.7 ***

Note: Statistical significance compared to the performance of intact animals:

* - $p < 0.05$; ** - $p < 0.01$; *** - $p < 0.001$.

Summarizing the results of the studies according to the dynamics of changes in indicators in the «elevated plus maze» test, we can say that after modeling atherosclerosis, certain changes in the increase in anxiety of the studied rats were revealed (reduction in the number of hanging from open sleeves, the number of vertical stands and looks from closed sleeves, the number of grooming reactions), which after the start of poisoning with nickel nitrate increased even more in subsequent periods of poisoning. There was exhaustion of the animals and a sharp suppression of

behavioral reactions, the maximum disturbances of which were observed two months after poisoning. Moreover, as the poisoning period increased, the animals lost weight and consumed little amounts of water.

The obtained data indicate the suppressive effect of chronic poisoning with nickel nitrate on the state of the central nervous system of experimental animals. The toxic neurotropic effect of chronic intoxication with nickel nitrate in experimental atherosclerosis dictates the need to develop effective methods of correction in the clinic of chronic poisoning with nickel nitrate,

which is especially important for people of older age groups and patients with atherosclerotic vascular lesions.

CONCLUSION

1. Modeling atherosclerosis led to an increase in anxiety in experimental rats.

2. Poisoning with nickel nitrate after modeling atherosclerosis aggravated the state of anxiety, and at the end of 60 days, there was a suppression of behavioral reactions, which indicated the toxic neurotropic effect of chronic intoxication with nickel nitrate against the background of atherosclerotic changes.

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ЭТОЛОГИЧЕСКОЕ ИССЛЕДОВАНИЕ СОСТОЯНИЯ ТРЕВОЖНОСТИ У КРЫС ПРИ ХРОНИЧЕСКОЙ ЗАТРАВКЕ НИТРАТОМ НИКЕЛЯ НА ФОНЕ ЭКСПЕРИМЕНТАЛЬНОГО АТЕРОСКЛЕРОЗА

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Целью исследования являлось изучение влияния хронической затравки нитратом никеля при экспериментальном атеросклерозе на состояние тревожности в тесте «приподнятый крестообразный лабиринт». Эксперименты проведены на 50 белых нелинейных крысах-самцах. Модель атеросклероза создана по И.В. Савицкому с соавт. (2016), которая основана на полиэтиологической теории развития заболевания. После моделирования атеросклероза затравку нитратом никеля проводили через питьевую воду поилок в течении 60 дней в дозе 2 мг/кг.

Полученные данные показали, что моделирование атеросклероза приводит к нарастанию состояния тревожности у экспериментальных крыс. Затравка нитратом никеля после моделирования атеросклероза усугубляет состояние тревожности и концу 60 суток отмечается подавление поведенческих реакций, что свидетельствует о токсическом нейротропном действии хронической интоксикации нитратом никеля на фоне атеросклеротических изменений. Полученные данные свидетельствуют о токсическом нейротропном эффекте хронической интоксикации нитратом никеля при экспериментальном атеросклерозе и подчеркивают необходимость разработки эффективных методов коррекции.

Ключевые слова: атеросклероз, нитратом никеля, приподнятый крестообразный лабиринт

EKSPERIMENTAL ATEROSKLEROZ FONUNDA NİKEL NİTRAT İLƏ XRONİKİ ZƏHƏRLƏNMƏ ZAMANI SIÇOVULLARIN NARAHATLIQ VƏZİYYƏTİNİN ETOLOJİ TƏDQİQİ

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Tədqiqatın məqsədi eksperimental aterosklerozda nikel nitrat ilə xroniki zəhərlənmənin «yüksəldilmiş xaçşəkilli labirint» testi vasitəsilə narahatlıq vəziyyətinə təsirini öyrənmək idi. Təcrübələr 50 ağ qeyri-xətti erkək siçovul üzərində aparılmışdır. Ateroskleroz modeli xəstəliyin inkişafının polietoloji nəzəriyyəsinə əsaslanan İ.V.Savitskiy və b. (2016) görə yaradılmışdır. Aterosklerozun modelləşdirilməsindən sonra 2 mq/kg dozada 60 gün ərzində içməli su vasitəsilə nikel nitrat ilə zəhərlənmə aparılmışdır.

Əldə edilən məlumatlar göstərdi ki, aterosklerozun modelləşdirilməsi eksperimental siçovullarda narahatlıq vəziyyətinin artmasına səbəb olur. Aterosklerozun modelləşdirilməsindən sonra nikel nitrat ilə zəhərlənmə isə narahatlıq vəziyyətini ağırlaşdırır və 60 günün sonunda aterosklerotik dəyişikliklər fonunda nikel nitrat ilə xroniki intoksikasiyanın zəhərli neyrotrop təsirini göstərən davranış reaksiyalarının tükənməsi qeyd edilmişdir. Əldə edilmiş nəticələr eksperimental aterosklerozda nikel nitrat ilə xroniki intoksikasiyanın toksik neyrotrop təsirini göstərir və effektiv korreksiya üsullarının işlənilib hazırlanmasının zəruriliyini vurğulayır.

Açar sözlər: ateroskleroz, nikel nitrat, yüksəlmiş xaçşəkilli labirint

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