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DEVELOPMENT OF OXIDATIVE STRESS AND INFLAMMATORY PROCESSES IN RATS UNDER NITRITE-TOBACCO INTOXICATION AND AFTER THE USE OF ENTEROSORPTION

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Intoxication rats of tobacco smoke was simulated in sealed chamber by burning 6 cigarettes (within 45 days). 24 and 72 hours before the end of the experiment, animals were injected with sodium nitrite at the dose of 45 mg/kg body weight, enterosorbent Carboline at the dose of 400 mg/kg (within 30 days). Increase in the content of met- and carboxyhemoglobin in rats' blood of all age groups during the experiment was noted. Immature rats were the most sensitive to simultaneous toxicant damage. The blood serum of affected old rats showed the highest content of C-reactive protein (3.3 times higher than the normal). Carboline had most effect on this index at the end of the study. In blood serum of affected rats in all age groups, shift in the cytokine balance towards pro-inflammatory processes was observed (increase in the content of interleukin-6 and decrease in interleukin-4). Enterosorbent had the most effect on the cytokine balance in mature rats.

Key words: nitrite-tobacco intoxication, meth- and carboxyhemoglobin, cytokines, C-reactive protein

The work is a fragment of the research project "Biochemical mechanisms of metabolic disorders under the conditions of administering toxicants of different genesis", state registration No. 0115U003359.

Smoking is a socio-economic phenomenon and one of the important health problems in Ukraine and around the world, as it is available to everybody and is therefore widespread. The spread of smoking in Ukraine is a significant threat to public health, the cause of disability and pre-terminal death [5]. Active and passive tobacco smoking can cause the formation of many active forms of oxygen - hydrogen peroxide, epoxides, nitrogen oxide (NO), nitrogen dioxide, peroxyntirite (ONOO-). The latter activate the processes of free radical oxidation in the body. Exposure to cigarette smoke is known to activate circulating immunocytes in the lungs, which then release pro-inflammatory cytokines. Cytokines are formed by almost all cells of the body for intercellular interaction and regulation of biochemical processes in the cell [8]. Important role in the pathogenesis of toxic lesions in the body is given to the imbalance of cytokines.

A significant environmental and medical-biological problem in the agro-industrial regions of Ukraine is the combined effect on the human and animal body of inorganic nitro compounds, which is accompanied by cases of nitrate-nitrite intoxication. Under the influence of sodium nitrite, the first link in the pathogenesis is hemoglobin. The effect of sodium nitrite is manifested primarily in the oxidation of oxyhemoglobin to methemoglobin (MetHb) and a sharp increase in the intensity of free radical reactions [4].

Due to the summation of environmental risk factors, a chronic inflammatory process can occur, in which all organs and tissues are involved.

The growing number of diseases and pathological conditions, where a significant role is played by disorders of oxidative processes, immune and inflammatory responses, causes the emergence and deepening of endogenous intoxication manifestations.

The way out of this situation can be the widest possible and at the same time careful involvement of enterosorbents in treatment and prevention measures. Among the significant number of sorbents currently used in clinical practice, a significant place belongs to the "Carboline" drug. It is an inorganic, multifunctional enterosorbent based on tissue carbon fiber, which exhibits pronounced sorption and detoxification properties [1].

The purpose of this work was to study the content of hemoglobin derivatives and cytokine balance in rats of different ages with tobacco nitrite intoxication after enterosorption.

Materials and methods. The experiments were performed on white outbred male rats, which were kept on the standard diet of the vivarium of Ternopil National Medical University. Rats are divided into three age categories: the first - immature with a body weight of 60-80 g, the second - mature with a body weight of 180-200 g, the third - old rats with a body weight of 300-320 g. Each age group consisted of two subgroups - intact control and research group. The rats of the experimental groups were exposed to tobacco smoke for 45 days. Experimental animals were divided into 4 more groups. One of them was administered sodium nitrite at the dose of 45 mg/kg body weight 24 h before the end of the experiment, the other was administered sodium nitrite 72 h before euthanasia. Two more groups after being damaged with the both toxicants were intragastrically administered Carboline enterosorbent at the dose of 400 mg/kg body weight for 30 days (starting from the 15th day of tobacco smoke intoxication and daily until the end of the experiment) [1]. The model of chronic exposure to tobacco smoke was implemented using a airtight

chamber with a capacity of 30 liters, which permitted to fumigate the animals in free behavior. Tobacco smoke from the burning of 6 Prima Silver (Blue) cigarettes (containing 0.6 mg of nicotine and 8 mg of tar) was delivered into the chamber through openings. There were simultaneously 6 animals in the chamber for 6 minutes. Animals of the control group were also kept in the airtight chamber for 6 minutes, but were not exposed to tobacco smoke [9]. 45 days after the onset of tobacco smoke, exposure, the animals were sacrificed by euthanasia under thiopental anesthesia.

In our study we used the general principles of animal experiments, consistent with the provisions of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes [11].

Blood and serum were sampled for the study. The content of methemoglobin (MetHb) in the reaction with acetone cyanhydrin [7] and carboxyhemoglobin (HbCO) in the reaction with potassium hexacyanoferrate (III) was determined in the blood [2]. Enzyme-linked immunosorbent assay was used to determine the level of proinflammatory cytokine, interleukin 6 (IL-6) [8] and anti-inflammatory - interleukin 4 (IL-4) [13]. The concentration of these cytokines in the serum of peripheral blood was assessed by solid-phase enzyme-linked immunosorbent assay with the RT-2100C immunoassay analyser. Test systems and control sera IL-6 and IL-4 produced by the manufacturer (Russia) were used in compliance with the relevant protocols to the test systems. To determine the concentration of cytokines the ULAB-108UA spectrophotometer was used, the wavelength being 450 nm. The concentration of cytokines studied according to the calibration curve of the respective standards was expressed in picograms per 1 ml of blood serum (pg/ml). The content of C-reactive protein (C-RP) was determined by the turbidimetric method, the principle of which is the appearance of turbidity due to the formation of insoluble immunocomplexes antigen-antibody (latex agglutination reaction). The intensity of the turbid solutions formation is recorded at 340 nm [10].

Statistical processing of the obtained data was performed using the program "STATISTICA 6.0" using the ANOVA parametric criterion and nonparametric Wilcoxon test for related samples. The changes were considered reliable at $p \leq 0.05$ [6].

Results of the study and their discussion. It is known that nitrate-containing compounds, as strong oxidants, have an effect on hematological parameters, converting bivalent heme ferrum into trivalent, forming a pathological form of hemoglobin - methemoglobin (MetHb) or hemoglobin, which is unable to reverse the addition of oxygen, which further causes hypoxia and is the main marker of the intoxication severity with nitrogen-containing compounds [4].

Prolonged smoking changes the oxygen balance of the blood and the utilization of oxygen by tissues. Carbon monoxide blocks myoglobin and impairs oxygen transport to mitochondria. The concentration of methemoglobin (HbCO) in the blood grows, which contributes to the development of acute circulatory failure of muscle tissue, tissue hypoxia, damage to vascular cells and increasing risk of atherosclerotic changes in blood vessels of all diameters [5].

Study on the content of MetHb in the blood of rats affected by sodium nitrite against the background of tobacco intoxication, showed its increase in all age groups during the experiment. After the damage with the both toxicants, the most sensitive were immature rats, in which this index increased sharply and was the highest by the end of the experiment – by 3.3 times higher compared to the control animals (table 1).

Table 1

Content of methemoglobin and carboxyhemoglobin (g/l) in the blood of different ages rats affected by sodium nitrite against the background of tobacco intoxication, and after the use of Carboline enterosorbent ($M \pm m$; $n = 6$)

Term of study, day/hours	Groups of experimental animals		
	Immature rats	Mature rats	Senile rats
	Methemoglobin		
Control rats	1.53±0.14	1.50±0.15	1.41±0.07
45 day of TS+24 hours SN	4.53±0.15*	3.64±0.09*	3.98±0.11*
45 day of TS+24 hours SN +Carboline	3.64±0.09**	3.37±0.09	3.49±0.06**
45 day of TS+72 hours SN	5.02±0.18*	4.01±0.20*	4.10±0.17
45 day of TS+72 hours SN +Carboline	3.85±0.15**	3.55±0.12	3.64±0.09
	Carboxyhemoglobin		
Control rats	0.0148±0.0012	0.0207±0.0016	0.0188±0.0017
45 day of TS+24 hours SN	0.0428±0.0040*	0.0328±0.0028*	0.0408±0.0026*
45 day of TS+24 hours SN +Carboline	0.0402±0.0029	0.0293±0.0025	0.0358±0.0028
45 day of TS+72 hours SN	0.0448±0.0038*	0.0311±0.0022*	0.0437±0.0035*
45 day of TS+72 hours SN +Carboline	0.0387±0.0019	0.0273±0.0022	0.0391±0.0032

Note: * - reliable changes between control and toxic animals; ** - reliable changes between affected rats and rats receiving carboline; TS - tobacco smoke; SN - sodium nitrite.

During this term of the study, the content of MetHb in the blood of mature rats increased by 2.7 times, in senile rats - by 2.6 times, compared to the level of control animals.

After the use of Carboline, the content of MetHb in the blood of immature animals decreased by 76%. Carboline had a similar effect on the process of methemoglobin formation in the groups of mature and senile rats.

One more index that characterizes the pathological changes in the body of animals after exposure to tobacco smoke and contributes to the deepening of hypoxia is carboxyhemoglobin. Carbonyl, or carbon monoxide contained in tobacco smoke, has the ability to bind the respiratory pigment of blood - hemoglobin. The resulting carboxyhemoglobin is not able to carry oxygen; as a result, tissue respiration processes are impaired [2].

By the end of the experiment, the HbCO content in the blood of immature rats (under the action of the both toxicants) has increased the most - by 3 times higher than the normal, in mature rats - by 1.5 times and in the senile - by 2.3 times higher than the level of animals in the control group.

When Carboline was used for 30 days, a tendency to decrease the carboxyhemoglobin content in the affected rats was observed, but no reliable changes were observed in any study period in all age groups of animals.

Therefore, the results obtained permit to note that the most sensitive to the simultaneous damage by sodium nitrite and tobacco smoke are immature rats, in which the content of methemoglobin and carboxyhemoglobin after the exposure is the highest. The Carboline enterosorbent used by us selectively had a positive effect on these indices in rats of different age groups.

The key mechanism for the development of lung diseases is inflammation, which occurs under the influence of various non-specific stimuli (tobacco smoke, air pollutants, etc.). Pulmonary inflammation, mediated by the accumulation of various cells (neutrophils, macrophages), is accompanied by oxidative stress, which supports inflammation [3].

The study of C-protein content is one of the most acceptable markers of early diagnosis and monitoring of inflammatory disease [3]. C-RP is a representative of several functional groups: mediators, transport proteins, immunomodulators. It is a highly sensitive but nonspecific acute phase index that is produced in response to most forms of tissue damage, infection, or inflammation.

We have studied the content of C-RP in the blood serum of rats in different age groups affected by sodium nitrite against the background of tobacco intoxication. The highest content of this index was registered in the blood serum of senile rats, in which by the end of the experiment it increased by 3.3 times (fig. 1).

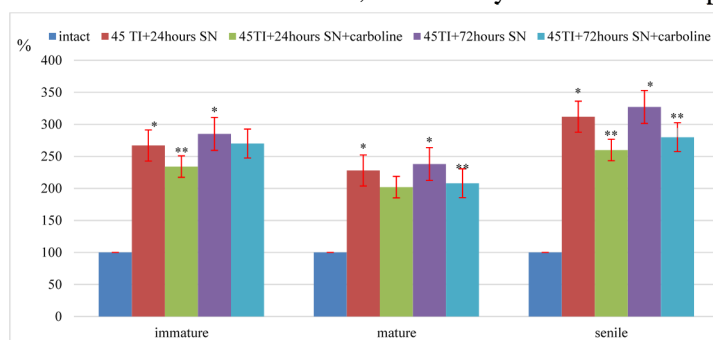


Fig.1. Content of C-reactive protein in the blood serum of rats at different ages under conditions of nitrite-tobacco intoxication and after the use of Carboline, %.

Note: * - reliable changes between control and toxicant affected animals; ** - reliable changes between affected rats and rats receiving carboline.

It is known that the synthesis and secretion of C-RP takes place in the liver and is regulated by proinflammatory cytokines, primarily by IL-6, but it can be produced by macrophages, lymphocytes. It should be noted that the peak concentration of C-RP correlates with the maximum increase in the concentration of IL-6 [12].

Based on the above, it was advisable to study the cytokine balance in smoke-toxicated and sodium nitrite-affected rats of different ages. Damage of rats with sodium nitrite against the background of 45-day intoxication of TS led to an increase in the content of proinflammatory cytokine IL-6 in the blood serum of rats in all experimental groups (table 2).

The highest content of IL-6 was observed in the serum of immature rats, which increased by 4.6 times at the end of the experiment. By the end of the experiment, after the damage induced by both toxicants, the content of proinflammatory cytokine in the blood serum of mature rats increased by 3.5 times, in the senile - by 2.6 times compared to the intact control group.

From the data presented in fig. 1 it can be seen that throughout the experiment, the content of C-RP increased. Carboline was effective at the late stages of the study (under its influence, the content of C-RP reliably decreased in this group of animals). Similar changes in the C-RP content were observed in the blood serum of immature and mature rats after the induced damage and carboline administration. More resistant to such changes were mature rats, in which this index increased the least after the damage.

Content of pro-inflammatory IL-6 and anti-inflammatory IL-4 (pg/l) in the blood serum of rats at different ages affected by sodium nitrite against the background of tobacco intoxication, and after the use of Carboline enterosorbent ($M \pm m$; $n = 6$)

Term of study, day/hours	Groups of experimental animals		
	Immature rats	Mature rats	Senile rats
	proinflammatory IL-6		
Control rats	1.91±0.28	3.00±0.30	4.14±0.17
45 day of TS+24 hours SN	7.74±0.35*	9.35±0.32*	10.94±0.21*
45 day of TS+24 hours SN +Carboline	6.96±0.20	8.77±0.13	9.88±0.29**
45 day of TS+72 hours SN	8.87±0.21*	10.50±0.26*	10.90±0.31*
45 day of TS+72 hours SN +Carboline	7.89±0.34	8.94±0.23**	9.11±0.23**
	anti-inflammatory IL-4		
Control rats	1.98±0.04	1.45±0.03	1.36±0.02
45 day of TS+24 hours SN	1.13±0.04*	1.02±0.03*	0.90±0.03*
45 day of TS+24 hours SN +Carboline	1.14±0.02	1.08±0.03	0.96±0.04
45 day of TS+72 hours SN	0.90±0.02*	0.85±0.03*	0.75±0.02*
45 day of TS+72 hours SN +Carboline	0.96±0.02	0.96±0.04**	0.77±0.03

Note: * - reliable changes between control and toxicated animals; ** - reliable changes between affected rats and rats receiving carboline.

Efficacy of Carboline used was manifested mainly in the groups of mature and senile rats, in the blood serum of which by the end of the experiment the content of IL-6 reliably decreased ($p \leq 0.05$).

The basis for the development of the inflammatory process is the launch of the cytokine cascade, which includes, on the one hand, pro-inflammatory cytokines, on the other hand - anti-inflammatory mediators. The balance between the two oppositely directed groups of cytokines, mainly, determines the nature of the course and outcome of the disease. IL-4 has been shown to have a potent anti-inflammatory effect and plays a key role in the inflammatory response, as well as reducing the inflammatory functions of monocytes and macrophages.

We studied the content of IL-4 in the blood serum of rats affected by sodium nitrite against the background of tobacco intoxication, and the effect of the Carboline enterosorbent drug (table 2).

By the end of the study, the content of anti-inflammatory cytokine was most pronounced in the blood serum of immature rats - by 2.2 times, while in mature and senile rats - by 1.7 and 1.8 times, respectively (compared to the control).

Carboline did not show a positive effect on this index in the groups of immature and senile animals. In the group of mature rats, the content of IL-4 in the blood serum reliably increased ($p \leq 0.05$).

Oxidative stress and accumulation of toxic products of exogenous and endogenous origin in the body of affected rats, which we had found before, led to the development of inflammatory processes with their deepening depending on the age of the animals. This is confirmed by an imbalance of pro- and anti-inflammatory cytokines and an increase of the acute phase protein - C-reactive protein in the blood serum.

Our data are consistent with the literature [15], which shows that smokers have an impairment of the hemoglobin transport function in the blood, and in particular, an increase in oxygen-inactive forms of hemoglobin, particularly ligands such as methemoglobin and sulfhemoglobin. In addition, nitrate-containing compounds, as strong oxidants, have an effect on hematological parameters, forming a pathological form of hemoglobin - methemoglobin [14]. Some authors attribute a significant role in the development of metabolic disorders under the influence of cigarette smoke to carbon monoxide and oxidizing gases. Carbon monoxide reduces the transport of oxygen in the blood and its availability to the myocardium by increasing the level of carboxyhemoglobin in the blood [5], which is consistent with the observed increase in meth- and carboxyhemoglobin under the conditions of rats' damage with sodium nitrite against tobacco intoxication.

There is evidence suggesting that tobacco smoke can cause inflammation, in particular through the induction of pro-inflammatory cytokines. Proinflammatory cytokines are produced mainly by activated macrophages and are involved in the regulation of inflammatory reactions [15]. The observed increase in the content of interleukin-6 and decrease in the content of interleukin-4 under the conditions of nitrite-tobacco intoxication confirms the literature data on the imbalance in the content of pro- and anti-inflammatory cytokines in smokers.

Among the biomarkers that reflect changes in inflammation, acute phase proteins that appear in blood plasma 4-6 hours after tissue damage by various factors, including C-reactive protein, are of great importance [10]. We noted a reliable increase in this index in the blood serum of rats in our experiment, which was more pronounced in senile animals.

The use of Carboline enterosorbent was effective in nitrite-tobacco intoxication, which, in our opinion, indirectly affected the hematological parameters and led to the suppression of inflammatory activity in the toxicated body.

Conclusions

1. Simultaneous damage to rats induced with sodium nitrite and tobacco smoke leads to the activation of free radical processes, as indicated by the increased content of methemoglobin in the blood of rats at all ages. Along with this, there is an increase in carboxyhemoglobin in animals of different ages. Immature rats were the most sensitive to toxicants. Immature rats were sensitive to the effects of the Carboline enterosorbent (probably, the methemoglobin content decreased, which is a consequence of the free radical process activation after the damage).

2. Under the conditions of nitrite-tobacco intoxication in the blood serum probably the content of C-reactive protein increased, which was most pronounced in senile animals. In addition, there was a shift in the balance between cytokines towards pro-inflammatory processes, as indicated by an increase in the content of pro-inflammatory interleukin and a decrease in the content of anti-inflammatory interleukin after the damage. Carboline was effective in influencing C-reactive protein content in immature and senile rats, probably reducing it at the end of the study. In mature rats, enterosorbent led to a probable restoration of serum cytokine imbalance after intoxication with both toxicants.

3. The obtained results confirmed the possibility of including Carboline enterosorbent in complex treatment regimens for intoxications caused by chemical compounds, as well as by smoking.

References

1. Andreychyn SM, Lototska SV. Efektyvnist zastosuvannya enterosorbentu «Karbolayn» pry likuvanni khvorykh na khronichne obstruktyvne zakhvoryuvannya lehen. Journal of Education, Health and Sport. 2015; 5(5):125-130. doi: 10.5281/zenodo.17463. [in Ukrainian]
2. Velyhotsky DV, Stelmakh NV, Mamilov SO, Yesman SS. Aparatno-prohramnyyy kompleks dlya neinvazyvnoho diahnozuvannya karboksyhemoglobinu v potokakh krovi. Visnyk KrNU imeni Mykhayla Ostrohradskoho. 2012; 72(1):71-74. [in Ukrainian]
3. Volkova LI, Timofeyeva AV. C-reaktivnyy belok kak pokazatel sistemnogo vospaleniya u bolnykh khronicheskoy obstruktyvnoy boleznyu legkikh. Sovremennyye problemy nauki i obrazovaniya. 2013; 6:122-138. [in Russian]
4. Hunchak VM. Do toksykolohiyi nitrativ i nitrytiv u tvaryn. Naukovyy visnyk LNUVMBT imeni SZ. Hzhyskoho. 2013; 57(3):62-70. [in Ukrainian]
5. Kvasha NA. Meditsynskiye aspekty tabakokureniya. Zdorovya Ukrayiny. 2010; 20(249):40-41. [in Russian]
6. Shelamova MA, Insarova NI, Leshchenko VG. Statisticheskyy analiz mediko-biologicheskikh dannykh s ispolzovaniyem programmy EXCEL. Minsk: BGMU. 2010; 96 s. [in Russian]
7. Arakaki LS, Ciesielski WA, Thackray BD, Feigl EO, Schenkman KA. Simultaneous Optical Spectroscopic Measurement of Hemoglobin and Myoglobin Saturations and Cytochrome aa3 Oxidation In Vivo. Appl Spectrosc. 2010; 64(9): 973-979. doi: 10.1366/000370210792434387.
8. Chen Z, Li R, Xie Z, Huang G, Yuan Q, Zeng J. IL-6, IL-10 and IL-13 are associated with pathogenesis in children with Enterovirus 71 infection. Int. J. Clin. Exp. Med. 2014 Sep; 7(9):2718-2723.
9. Churg A, Wright J. Animal models of cigarette smoke-induced chronic obstructive pulmonary disease. Expert Rev Respir Med. 2010;4(6):723-34. doi: 10.1586/ers.10.68.
10. Deng ZC, Zhao P, Cao C, Sun SF, Zhao F, Lu CY, et al. C-reactive protein as a prognostic marker in chronic obstructive pulmonary disease. Exp Ther Med 2014; 7:443-6. doi: 10.3892/etm.2013.1441.
11. Gross D, Tolba RH. Ethics in Animal-Based Research. Eur Surg Res. 2015 Apr; 55(1-2), 43-57. doi:10.1159/000377721.
12. Hubeau C, Kubera JE, Masek-Hammerman K, Williams CM. Interleukin-6 neutralization alleviates pulmonary inflammation in mice exposed to cigarette smoke and poly(I:C). Clin. Sci.(Lond). 2013 Nov; 125:483-493. doi: 10.1042/CS20130110.
13. Nam J, Park K, Park E, Lee YB, Lee HG, Baik HH, et al. Interleukin-13/-4-induced oxidative stress contributes to death of hippocampal neurons in $\alpha\beta 1$ -42-treated hippocampus in vivo. Antioxid Redox Signal. 2012 Jun; 16(12):1369-83. doi: 10.1089/ars.2011.4175.
14. Taylor CT, Moncada S. Nitric oxide, cytochrome c oxidase, and the cellular response to hypoxia. Arterioscler Thromb Vasc Biol. 2010 Apr; 30(4):643-7. doi: 10.1161/atvbaha.108.181628.
15. Wilson KM, Weggate SC, Pier J, Weis E, Love T, Evans K, et al. Secondhand smoke exposure and serum cytokine levels in healthy children. Cytokine. 2012 Oct; 60(1):34-7. doi: 10.1016/j.cyto.2012.06.236

Реферати

РОЗВИТОК ОКИСНОГО СТРЕСУ ТА ЗАПАЛЬНИХ ПРОЦЕСІВ В ОРГАНІЗМІ ЩУРІВ ЗА УМОВ НІТРИТНО-ТЮТЮНОВОЇ ІНТОКСИКАЦІЇ ТА ПІСЛЯ ЗАСТОСУВАННЯ ЕНТЕРОСОРБЦІЇ

Лихацький П.Г., Фіра Л.С., Івануса І.Б.

Ураження тютюновим димом моделювали у герметичній камері від горіння 6 сигарет протягом 6 хв (45 днів). За 24 та 72 год до закінчення експерименту тваринам вводили натрію нітрит у дозі 45 мг/кг маси тіла, ентеросорбент Карболайн - у дозі 400 мг/кг (30 днів). Відмічено збільшення вмісту мет- та карбоксигемоглобіну у крові щурів усіх вікових груп впродовж експерименту. Найбільш чутливими до

РАЗВИТИЕ ОКИСЛИТЕЛЬНОГО СТРЕССА И ВОСПАЛИТЕЛЬНЫХ ПРОЦЕССОВ В ОРГАНИЗМЕ КРЫС В УСЛОВИЯХ НИТРИТНО-ТАБАЧНОЙ ИНТОКСИКАЦИИ И ПОСЛЕ ПРИМЕНЕНИЯ ЭНТЕРОСОРБЦИИ

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Интоксикацию крыс табачным дымом моделировали в герметичной камере от горения 6 сигарет (45 дней). За 24 и 72 ч до окончания интоксикации животным вводили натрия нитрит в дозе 45 мг / кг массы тела, энтеросорбент Карболайн - в дозе 400 мг / кг (30 дней). Отмечено увеличение содержания мет- и карбоксигемоглобина в крови крыс всех возрастных групп на протяжении эксперимента. Наиболее чувствительными к

одночасного ураження токсикантами є статевонезрілі шури. Найвищий вміст С-реактивного протеїну зареєстровано у сироватці крові шурів старечого віку, у яких він підвищився в 3,3 раза. Карболайн виявився ефективним в останні терміни дослідження. Після ураження спостерігався зсув балансу між цитокинами в сторону прозапальних процесів, на що вказувало підвищення вмісту прозапального та зниження вмісту протизапального інтерлейкіну. У статевозрілих шурів ентеросорбент призвів до вірогідного відновлення дисбалансу цитокинів у сироватці крові після ураження.

Ключові слова: натрію нітрит, тютюновий дим, метгемоглобін, карбоксигемоглобін, цитокини, С-реактивний протеїн

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одновременному поражению токсикантами были неполовозрелые крысы. В сыворотке крови пораженных старых крыс отмечено наиболее высокое содержание С-реактивного протеина (в 3,3 раза выше нормы). Карболайн оказал эффективное влияние на этот показатель в конце исследования. В сыворотке крови пораженных крыс всех возрастных групп наблюдался сдвиг цитокинового баланса в сторону провоспалительных процессов (повышение содержания интерлейкина-6 и снижение интерлейкина-4). Наиболее эффективное влияние оказал энтеросорбент на цитокиновый баланс у половозрелых крыс.

Ключевые слова: нитритно-табачная интоксикация, мет- и карбоксигемоглобин, цитокины, С-реактивный протеин

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BIOCHEMICAL FEATURES OF POSTOPERATIVE SKIN WOUNDS HEALING AGAINST THE BACKGROUND OF DIABETES MELLITUS IN RATS WITH DIFFERENT WAYS OF WOUND CLOSURE

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The study is devoted to identifying the features of free radical processes changes in skin homogenate of the rats with diabetes mellitus, after using different methods of surgical wounds closing. Analysis of the results suggests that the use of skin glue significantly reduces the intensity of the free radical oxidation course in the cells of scarred skin tissues in animals with simulated diabetes mellitus compared to the application of nodal sutures to the wound under similar conditions.

Key words: free radical oxidation, oxidative stress, abnormal scar.

The work is a fragment of the research project "Systemic and organ disorders due to emergency factors effect on the body, mechanisms of their development and pathogenetic correction", state registration No. 016U003390.

Diabetes mellitus (DM) is considered to be one of the most important non-communicable diseases worldwide and is also one of the global health challenges of the 21st century [3]. It ranks fourth among the major causes of death in developed countries [15].

In 2017, 1,270,929 cases of diabetes were registered in Ukraine. Today, almost 50% of diabetes cases are undiagnosed. Development of late complications leads to a significant reduction in quality of life, reducing its duration by 10-30%, disability, increased mortality of patients by 2-3 times and significant budget expenditures for their treatment. The number of patients with diabetes mellitus is increasing by 5-7% annually. Such indices indicate a non-infectious epidemic of diabetes.

Wound healing is a coordinated process that goes through certain stages with different types of cells and their waste products participating, which regulate the healing process. It is proved that in patients with DM there is the wound healing process disorder, but not all features of this process in diabetes mellitus are completely understood.

At the same time, the quality and structure of the material, the chemical composition of the suture material effect the reaction of tissues to their introduction, as well as the final result of the operation. Free radical oxidation (FRO) is an important biochemical conversion process of lipids, proteins, nucleic acids and other compounds under the action of free radicals, and peroxide oxidation of lipids (LPO) and proteins is one of the further consequences [2, 13]. At all stages of the FRO, due to the interaction of free radicals and biological macromolecules, numerous intermediate products are formed. Such peroxidation compounds, in their excess, are characterized by pronounced cytotoxic activity. As a result, the processes of energy production in the cell are suppressed, the synthesis of proteins and nucleic acids is disrupted, which in its turn leads to the formation of pathological scar tissue.

The purpose of the study to identify the features of free radical processes changes in the skin homogenate of rats in different ways of surgical wounds closing, in the conditions of diabetes mellitus.

Materials and methods. An experiment was performed on 60 adult male rats weighing 240-280 g. The rats were simulated diabetes mellitus by intraperitoneal administration of streptozotocin