ORIGINAL ARTICLE

CONTENTS

Impact of cranioskeletal trauma on the development of endogenous intoxication syndrome in rats of different ages

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ABSTRACT

Aim: The aim of the study was to determine the impact of cranioskeletal trauma (CST) on the development of endogenous intoxication syndrome in rats of different ages.

Materials and Methods: The experiments involved 147 white male Wistar rats of different age groups. The first experimental group included sexual immature rats aged 100-120 days. The second group includes sexually mature rats aged 6-8 months. The third group included old rats aged 19-23 months. In all experimental groups, CST was modelled under thiopentalonatrium anaesthesia. The control rats were only injected with thiopentalonatrium anaesthesia. The animals were withdrawn from the experiments under anaesthesia after 1, 3, 7, 14, 21 and 28 days by total bleeding from the heart. In blood serum, the content of fractions of molecules of middle mass was determined at a wavelength of 254 and 280 nm (MMM_{254}, MMM_{280}).

Results: As a result application of CST in rats of different age groups, an increase in the serum content of MMM_{254} and MMM_{280} was observed with a maximum after 14 days and a subsequent decrease by 28 days. At all times of the experiment, the indicators were statistically significantly higher compared to the control groups. The degree of growth of the MMM_{254} fraction after 1, 7 and 14 days was statistically significantly higher in sexual immature rats, and after 21 and 28 days – in old rats. In old rats after 21 and 28 days of the post-traumatic period, the content and degree of growth of the MMM_{280} fraction in the blood serum were also significantly higher.

Conclusions: Modelling of CST in rats of different age groups is accompanied by the development of endogenous intoxication syndrome, which is manifested by the accumulation of MMM_{254} and MMM_{280} fractions in the blood serum with a maximum after 14 days of the experiment. The content of the serum fraction of MMM_{254} in sexual immature rats in the dynamics of experimental CST exceeds other age groups after 1, 7 and 14 days, in old rats the content of the studied MMM fractions is significantly higher after 21-28 days.

KEY WORDS: traumatic brain injury, skeletal injury, endogenous intoxication of the kidney, age, molecular of middle mass

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INTRODUCTION

Traumatic brain injury (TBI) in the structure of polytrauma trauma is a serious problem for health care [1]. Despite the creation of specialized department of trauma and intensive care units, which has led to a reduction in mortality in polytrauma from exsanguination, acute respiratory distress syndrome and multiple organ dysfunction syndrome, TBI-related mortality remains the most common cause of death in trauma [2, 3]. It has been proven that the severity of TBI is the dominant factor in the mortality of victims with polytrauma [4].

Combined trauma contributes to the worsening of secondary brain damage. It is based on coagulopathy, hypotension, fever and hypoxia, which initiate a sequence of ischemic and damaging biochemical processes [5].

Age has been shown to be an independent predictor of TBI mortality. In older people, the frequency and severity of brain injury is associated with deterioration in motor and physiological functions, a higher risk of low-energy falls, and the appearance of intracranial hematomas with slow exacerbation [6], while younger patients usually suffer injuries related to sports, work, and road accidents and are more prone to polytrauma [7]. The age characteristics of patients, mechanisms of injury, and kinetics of brain damage emphasise the difficulties of approaches to TBI [8], which requires further in-depth study of the pathogenesis of combined cranioskeletal trauma (CST) in the age-related aspect.

As a result of physical trauma, there are disorders of the protective layers of the skin, fascia, capsules and underlying tissues. These injuries lead to the gener-

ation and release of damage-associated molecular fragments, including membrane debris, mitochondrial components, histones, DNA and RNA fragments, and damaged proteins [9]. Together with the products of normal and impaired metabolism, trauma results in the formation of a toxic excess of biologically active substances of molecular of middle mass (MMM) of 300-5000 daltons. As shown in the study [10], an increase in the concentration of MMM is one of the markers of the transition of the inflammatory toxic stage of endogenous intoxication syndrome in TBI to the stage of systemic endogenous intoxication. However, in the age aspect, the dynamics of the content of MMM in the blood under conditions of CST has not been studied.

AIM

To determine the effect of CST on the development of endogenous intoxication syndrome in rats of different ages

MATERIALS AND METHODS

The experiments were performed out on 147 white male Wistar rats of different age groups, which were selected randomly and kept on a standard vivarium diet. The first experimental group included sexually immature rats aged 100-120 days and weighing 90-110 g. The second group included sexually mature rats aged 6-8 months and weighing 180-200 g. The third group included old rats aged 19-23 months and weighing 300-320 g.

In all experimental groups (49 rats each), according to the method described in the study [10], CST was modelled under thiopentalonatrium anaesthesia (40 $mg \cdot kg^{-1}$). To modelling skeletal trauma - a closed fracture of the femur, sexual immature rats were firstly subjected to a dosed mechanical impact with a steel object with a wedge-shaped nozzle on the projection of the middle third of the left femur with an energy of 0.320 J, sexually mature rats - with an energy of 0.637 J, and old rats - with an energy of 0.796 J. Next, a dosed blow to the skull was applied with a blunt object to sexual immature rats at a point 3 mm anterior to the interaural line with an energy of 0.226 J, to sexual mature rats at a point 5 cm anterior to the interaural line with an energy of 0.375 J, and to old rats at a point 6 mm anterior to the interaural line with an energy of 0.549 J. Impact energy caused moderate TBI in animals of different age groups. No animals with penetrating skull damage or open femur fracture were used in the experiments. In the control groups (7 rats each), animals were only put under thiopentalonatrium anaesthesia.

The rats were withdrawn from the experiments under anaesthesia after 1, 3, 7, 14, 21 and 28 days by total bleeding from the heart. In blood serum, the content of individual fractions of MMM was studied at 254 nm (MMM_{254}, peptide fraction) and 280 nm (MMM_{280}, chromatophore fraction) using an Ulab 108 UV spectrophotometer (China) [11].

The experiments were performed in accordance with the 'General Ethical Principles for Experiments on Animals' adopted by the First National Congress on Bioethics (Kyiv, 2001) and agreed with the provisions of the 'European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes' (Strasbourg, 1986), as well as the conclusion of the Bioethics Commission of the I. Ya. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine No. 72 of 06.01.2023.

The obtained digital material was processed in the STATISTICA software package (StatSoft Inc., USA). The median (Me), lower and upper quartiles (LQ, UQ) were determined. For an independent comparison of the degree of deviation of indicators in animals of different age groups, the average ratio of individual values of the studied indicators to the average value of the control group was calculated [12]. The significance of differences was assessed by the nonparametric Mann-Whitney test.

RESULTS

As can be seen from Table 1, in the control groups of rats, the highest content of the fraction of MMM_{254} in the blood serum was observed in the group of sexually mature and old rats, which was 27.2 and 11.0 % higher, respectively, than in the group of sexually immature rats ($p_{1-2}<0.05$, $p_{1-3}<0.05$). In 1 day after the application of CST in the groups of experimental rats, the content of the MMM_{254} fraction in the blood serum increased significantly compared to the result of the control group - in sexually immature rats by 6.06 times ($p<0.05$), in mature rats – by 5.05 times ($p<0.05$), in old rats – by 4.71 times ($p<0.05$). The value of the studied index became statistically significantly higher in experimental groups 1 and 2 compared to experimental group 3 (by 15.9 and 22.8 %, respectively, p1-3<0.05, p2-3<0.05). Subsequently, after 3 days in the experimental groups of rats of different ages, the index significantly decreased compared to the result of day 1: in experimental group 1 – by 2.34 times ($p<0.05$), in experimental group 2 – by 2.25 times ($p<0.05$), in experimental group 3 - by 1.69 times ($p<0.05$), but in all experimental groups it remained statistically significantly higher than in the control (2.59, 2.24 and 2.79 times, respectively, $p<0.05$).

Under these conditions, the index in the group of old rats was significantly higher than in the group of sexually immature rats (by 19.6 %, $p_{1-3}<0.05$).

Further, up to 14 days, compared with the result of 3 days, the index in all experimental groups increased and reached the level of 1 day of the posttraumatic period ($p>0.05$), significantly exceeded the result of the control group ($p<0.05$) and significantly prevailed in the groups of sexually immature and mature rats compared with old rats ($p_{1-3}<0.05$, $p_{2-3}<0.05$). By day 28, the index in all experimental groups decreased. Compared with the result of the 14th day, the index in experimental group 1 decreased by 2.54 times ($p<0.05$), in experimental group 2 – by 3.27 times ($p<0.05$), in experimental group 3 – by 1.90 times ($p<0.05$), but in all experimental groups the index continued to remain significantly higher than in the control (respectively by 2.31, 1.46 and 2.62 times, $p<0.05$). At this time of the post-traumatic period in the group of old rats, the index was statistically significantly higher than in the groups of sexually immature and mature rats (by 24.1 and 57.1 %, respectively, $p_{1-3}<0.05$, $p_{2-3}<0.05$), and in the group of sexually immature rats it was significantly higher than in the group of sexually mature rats (by 26.6 %, $p_{1-2}<0.05$).

The analysis of the dynamics of the average ratio of individual values of MMM_{254} in the blood serum to the average value of the control group under the influence of cranioskeletal trauma in rats of different ages showed (Table 2) that 1 day after the application of CST, the index was significantly higher in experimental group 1 compared to experimental groups 2 and 3 (by 20.0 and 28.7 %, respectively, $p_{1-2}<0.05$, $p_{1-3}<0.05$). After 3 days, the index in all experimental groups decreased and was significantly higher in experimental group 3 compared to experimental group 2 (by 24.6 %, $p_{2-3}<0.05$). Up to 14 days, the index increased and at this time in experimental group 1 statistically significantly exceeded the result of experimental groups 2 and 3 (respectively by 25.4 and 19.9 % ($p_{1-2}<0.05$, $p_{1-3}<0.05$). Subsequently, the index decreased and after 28 days was significantly higher in experimental group 3 compared to experimental groups 1 and 2 (by 13.4 and 79.4 %, respectively, $p_{1-3}<0.05$, $p_{2-3}<0.05$). In experimental group 1, the index exceeded the result of experimental group 2 (by 58.2 %, $p_{1-2}<0.05$).

In turn, under the influence of CST, the content of the fraction of MMM_{280} in the blood serum (Table 3) in immature rats compared to the control also increased after 1 day of the experiment (by 44.2 %, $p<0.05$) and remained at the same level after 3 days ($p>0.05$). Subsequently, the index gradually increased up to day 14 of the experiment and at this time was 3.34 times higher than the control level ($p<0.05$) and was significantly higher than the result of the previous observation periods (2.32, 1.91 and 1.77 times, respectively, $p<0.05$). After 21 days, the index decreased, but the differences with respect to the result of the 14th day of the experiment were not statistically significant ($p>0.05$). Subsequently, after 28 days of the experiment, the index continued to decrease and was statistically significantly lower compared to the results of 14 and 21 days of the experiment ($p>0.05$), but remained significantly higher compared to the results of 1, 3 and 7 days of the experiment ($p<0.05$).

In sexually mature rats, the content of the MMM_{280} fraction in the blood serum under the influence of CST also increased compared to the control after 1 day of the experiment (by 77.7 %, $p<0.05$). Subsequently, the index continued to increase and reached the first "plateau" in 3-7 days. During these periods, the index was statistically significantly higher than the result of the 1st day of the experiment (by 13.5 and 16.1 %, respectively, $p<0.05$). After 14 and 21 days, the index continued to increase, reached the second "plateau" and exceeded the result of day 7 by 66.8 and 65.5 %, respectively ($p<0.05$). By day 28, the index decreased and was statistically significantly lower compared to the results of days 14 and 21 of the experiment ($p<0.05$), but significantly exceeded the results of days 1, 3 and 7 of the experiment ($p<0.05$).

In old rats, the content of the MMM_{280} fraction in the blood serum after modeling of CST increased by 65.0 % ($p<0.05$) compared to the control after 1 day of the experiment. Subsequently, the index after 3 and 7 days of the experiment continued to increase, reached the first "plateau" and was statistically significantly higher compared to the result of 1 day, respectively, by 45.6 and 45.9 % ($p<0.05$). Subsequently, the index gradually increased until day 21 of the experiment and was 55.7% higher compared to the result of day 7 of the experiment ($p<0.05$) and 17.4% higher compared to the result of day 14 ($p<0.05$). After 28 days, the index decreased and reached the level of day 14 ($p>0.05$). During this period of the experiment, the index was significantly lower compared to the result of 21 days ($p<0.05$), and statistically significantly higher than the result of 1, 3 and 7 days ($p<0.05$).

Comparison of the experimental groups showed that after 1, 3 and 14 days of the experiment, the differences in the content of the fraction of MMM_{280} in the blood serum were not statistically significant ($p_{1-2}>0.05$, $p_{1-3}>0.05$, $p_{2-3}>0.05$). At the same time, after 3, 7, 21 and 28 days of the experiment, the index was the highest in experimental group 3 and exceeded experimental group 1 by 35.7, 26.0, 24.0 and 33.9 %, respectively ($p_{1-3}<0.05$). After 3 and 28 days of the experiment, the

Table 1. The content of MMM_{254} in blood serum under the influence of cranioskeletal trauma in rats of different ages, Me (LQ;UQ) – median (lower and upper quartiles)

Animal Group	Control	Period after injury					
		1 day	3 day	7 day	14 day	21 day	28 day
Group 1 Sexually immature	0.136 (0.129; 0.138)	0.824* (0.788; 0.894) *	0.352*1 (0.320; 0.384) *1	0.559*1,3 (0.505; 0.580) *1,3	0.812*3,7 (0.771; 0.818) *3,7	0.353 (0.336; 0.386) *1,7,14	0.319 (0.287; 0.326) *1,7,14,21
Group 2 Sexually mature	0.173 (0.157; 0.196)	0.873 (0.822; 0.931) *	0.388 (0.365; 0.421) *1	0.556 (0.510; 0.590) *1,3	0.824 (0.805; 0.828) *3,7	0.377 (0.361; 0.401) *1,7,14	0.252 (0.239; 0.274) *1,3,7,14,21
Group 3 Old	0.151 (0.147; 0.166)	0.711 (0.672; 0.766) *	0.421 (0.390; 0.440) *1	0.542 (0.503; 0.602) *1,3	0.752 (0.748; 0.761) *3,7	0.452 (0.447; 0.471) *1,7,14	0.396 (0.391; 0.409) *1,7,14
p_{1-2}	<0.05	>0.05	>0.05	>0.05	>0.05	>0.05	<0.05
p_{1-3}	<0.05	<0.05	<0.05	>0.05	<0.05	<0.05	<0.05
p_{2-3}	<0.05	<0.05	>0.05	>0.05	<0.05	<0.05	<0.05

Notes. Here and in table 3:

1. * – differences in relation to the control group are statistically significant ($p<0.05$);
2. 1,3,7,14,21 – differences in the results of days 1, 3, 7, 14 and 21 of the experiment are statistically significant ($p<0,05$);
2. p_{1-2} – significance of differences between study groups 1 and 2;
3. p_{1-3} – significance of differences between study groups 1 and 3;
4. p_{2-3} – significance of differences between study groups 2 and 3.

Table 2. Dynamics of the average ratio of individual values of kidney MMM_{280} to the average value of the control group under the influence of cranioskeletal trauma in rats of different ages, Me (LQ;UQ) – median (lower and upper quartiles)

Animal Group	Control					
	1 day	3 day	7 day	14 day	21 day	28 day
Group 1 Sexually immature	6.06 (5.79; 6.57)	2.59 (2.35; 2.82)	4.11 (3.71; 4.26)	5.97 (5.67; 6.01)	2.60 (2.47; 2.84)	2.31 (2.11; 2.39)
Group 2 Sexually mature	5.05 (4,75; 5.38)	2.24 (2.11; 2.43)	3.21 (2.95; 3.41)	4.76 (4.65; 4.78)	2.18 (2.09; 2.32)	1.46 (1.38; 1.58)
Group 3 Old	4.71 (4.45; 5.07)	2.79 (2.58; 2.92)	3.59 (3.33; 3.99)	4.98 (4.95; 5.04)	2.99 (2.96; 3.12)	2.62 (2.59; 2.71)
p_{1-2}	<0.05	>0.05	<0.05	<0.05	<0.05	<0.05
p_{1-3}	<0.05	>0.05	>0.05	<0.05	<0.05	<0.05
p_{2-3}	>0.05	<0.05	>0.05	>0.05	<0.05	<0.05

Notes. Here and in table 4:

1. p_{1-2} – significance of differences between study groups 1 and 2;
2. p_{1-3} – significance of differences between study groups 1 and 3;
3. p_{2-3} – significance of differences between study groups 2 and 3.

index in experimental group 1 was also statistically significantly lower compared to experimental group 2 (by 9.4 and 9.2 %, respectively, $p_{1-2}<0.05$).

The dynamics of the average ratio of the individual values of the content of the fraction of MMM_{280} in the blood serum to the average value of the control group (Table 4) showed that the degree of growth of the studied indicator in all experimental groups after 1, 3 and 14 days of the experiment was almost the same ($p_{1-2}>0.05$, $p_{1-3}>0.05$, $p_{2-3}>0.05$). After 7, 21, and 28 days of experimentation, the degree of growth in experimental group 3 was statistically significantly higher

Table 3. The content of MMM_{254} in blood serum under the influence of cranioskeletal trauma in rats of different ages, Me (LQ;UQ) - median (lower and upper quartiles)

Animal Group	Control	Period after injury					
		1 day	3 day	7 day	14 day	21 day	28 day
Group 1 Sexually immature	0.226 (0.214; 0.245)	0.326 (0.319; 0.398) *	0.395 (0.374; 0.416) *	0.426 (0.410; 0.452) *1	0.755 (0.695; 0.795) *1,3,7	0.674 (0.600; 0.714) *1,3,7	0.502 (0.471; 0.527) *1,3,7,14,21
Group 2 Sexually mature	0.216 (0.206; 0.234)	0.384 (0.331; 0.399) *	0.436 (0.429; 0.460) *1	0.446 (0.433; 0.515) *1	0.744 (0.719; 0.756) *1,3,7	0.738 (0.705; 0.767) *1,3,7	0.553 (0.532; 0.591) *1,3,7,14,21
Group 3 Old	0.223 (0.212; 0.234)	0.368 (0.355; 0.399) *	0.536 (0.517; 0.564) *1	0.537 (0.515; 0.556) *1	0.712 (0.686; 0.750) *1,3,7	0.836 (0.793; 0.909) *1,3,7,14	0.672 (0.645; 0.692) *1,3,7,21
p_{1-2}	>0.05	>0.05	<0.05	>0.05	>0.05	>0.05	<0.05
p_{1-3}	>0.05	>0.05	<0.05	<0.05	>0.05	<0.05	<0.05
p_{2-3}	>0.05	>0.05	<0.05	>0.05	>0.05	<0.05	<0.05

Table 4. Dynamics of the average ratio of individual values of kidney MMM_{280} to the average value of the control group under the influence of cranioskeletal trauma in rats of different ages, Me (LQ;UQ) - median (lower and upper quartiles)

Animal Group	Control					
	1 day	3 day	7 day	14 day	21 day	28 day
Group 1 Sexually immature	1.44 (1.41; 1.76)	1.94 (1.89; 2.02)	1.88 (1.81; 2.00)	3.34 (3.07; 3.52)	2.98 (2.65; 3.16)	2.22 (2.08; 2.33)
Group 2 Sexually mature	1.78 (1.53; 1.84)	2.18 (2.13; 2.27)	2.06 (2.00; 2.38)	3.44 (3.33; 3.50)	3.42 (3.26; 3.55)	2.56 (2.46; 2.73)
Group 3 Old	1.65 (1.59; 1.79)	2.25 (2.12; 2.31)	2.41 (2.31; 2.49)	3.19 (3.08; 3.36)	3.75 (3.55; 4.08)	3.01 (2.89; 3.10)
p_{1-2}	>0.05	>0.05	>0.05	>0.05	<0.05	<0.05
p_{1-3}	>0.05	>0.05	<0.05	>0.05	<0.05	<0.05
p_{2-3}	>0.05	>0.05	>0.05	>0.05	<0.05	<0.05

compared to experimental group 1 (by 28.2, 25.8, and 35.6 %, respectively, $p_{1-3}<0.05$). Also, in study group 2, the index after 21 days was 14.8 % higher than in study group 1 ($p_{1-2}<0.05$), after 28 days – by 15.3 % ($p_{1-2}<0.05$).

DISCUSSION

The intensification of endogenous intoxication processes is one of the key syndromes of traumatic injury. According to the results of studies [13], one of the manifestations of endotoxemia in experimental moderate and severe TBI is the accumulation of MMM fractions in the blood serum. The dynamics of their content had a three-phase character: primary accumulation (3 hours after trauma), followed by a "plateau" period when the level of MMM did not change significantly (24-48 hours after trauma) and, finally, an avalanche-like accumulation of MMM starting from the 3rd day after trauma (72 hours – 5 days). The authors believe that the first stage is due to the entry of endotoxins into the bloodstream from damaged brain tissue (primary – "cerebral" posttraumatic endotoxemia). The reason for further stabilization of the level of endotoxemia could be the destruction of endotoxins and their excretion by the kidneys (the "plateau" period). At the third stage, a pronounced increase in all MMM fractions was noted, which is associated not only with the progression of nervous tissue damage but also with systemic damage to internal organs and tissues of the body due to the final formation of endogenous intoxication syndrome and multiple organ failure. According to data [14], increased endotoxicity is also characteristic of experimen-

tal skeletal trauma (fracture of both femurs). However, in the dynamics, the content of MMM fractions in the blood serum changed in a wave-like manner with a significant increase after 3 days of the experiment and a subsequent decrease by 7 days.

Work [15] showed that modeling of combined moderate TBI and skeletal trauma (femur fracture) in the acute period and the period of early manifestations of traumatic illness (1-7 days) causes a gradual increase in the content of MMM in the blood serum, indicating the leading role of TBI in the formation of endogenous intoxication syndrome in the conditions of CST.

Some studies have shown that after modeling of CST, the phenomena of endogenous intoxication do not subside even during the late manifestations of traumatic illness (14-35 days) [16]. The authors have shown that the content of serum fractions of MMM in the conditions of CST (moderate TBI and closed fracture of both femurs), the content of MMM fractions in the blood serum after 14 days of posttraumatic period significantly exceeds the control level, but by 21 days it increased even more, followed by a decrease by 35 days, which reached the control level. The authors conclude that in the period of late manifestations of traumatic disease in the body of experimental animals there are prerequisites for increasing the level of endotoxemia, which is primarily due to membrane-destructive and dysmetabolic processes.

Our studies have shown that in the acute period of traumatic illness (1 day) after modeling of CST, the content of the studied fractions of MMM increases in the blood serum compared to the control. At this stage, the serum is dominated by the content of the MMM_{254} fraction, which is considered a general integral indicator of the content of substances of low and medium molecular weight (from 500 to 5000 Da), which, in addition to peptides, include about 200 compounds of normal and abnormal metabolism [13]. Their appearance on the background of CST in the acute period of traumatic illness (1 day) is obviously due to the entry of endotoxins into the bloodstream from the damaged brain tissue, soft tissue, and femur of the injured limb. After 3 days, the index decreases, which indicates that the process of accumulation of endotoxins in the blood was balanced with the processes of their destruction and excretion from the body. However, later, after 7-14 days, the content of the MMM_{254} fraction in the blood serum increases again. During this period, the maximum increase in the concentration of the MMM_{280} fraction in the blood serum is also noted. Given that the MMM_{280} fraction characterizes an increase in the content of aromatic amino acids that are not normally formed, their accumulation, according to [13], may indicate systemic damage to internal organs. Subsequently, the content of the studied fractions of MMM gradually decreases and by day 28 does not reach the control level.

Analyzing the dynamics of the studied fractions of MMM in rats of different ages under the influence of CST, we first found that the degree of increase in the content of MMM_{254} fraction in the blood serum after 1 day significantly prevails in sexually immature rats compared to sexually mature and old rats. Consequently, the degree of destructive processes in the affected tissues of sexually immature rats is higher, which is obviously associated with more pronounced manifestations of hypermetabolism syndrome in this age group, which is characteristic of the acute period of traumatic illness [13]. Subsequently, after 3 days, the endotoxemia associated with the MMM_{254} fraction subsides, but its content does not reach the level of the control group. During this period, their lowest serum levels were observed in sexually mature rats, and the highest in old rats, which is obviously due to the different capacity of detoxification systems, which is lower in old rats. After 7 and 14 days, the rate increased again. The degree of increase is again significantly greater in sexually immature rats, with the lowest rate in sexually mature rats. It can be assumed that the repeated increase in the serum content of the MMM_{254} fraction in sexually immature rats is mainly due to secondary brain damage, which occurs in a delayed manner at a young age, due to the peculiarities of the structure of the skull (greater bone plasticity, wider subarachnoid space) and brain (greater tissue hydrophilicity) [17]. In other study groups, the increase in serum MMM_{254} fraction was due to venous damage to internal organs and the development of functional insufficiency of detoxification systems.

Subsequently, during the late manifestations of traumatic disease – after 21 and 28 days - the content of the fraction of MMM_{254} in the blood serum decreases, but does not reach the level of the control group and continues to remain significantly higher. At these times, the content of the fraction of MMM_{254} in the blood serum is statistically significantly higher in old rats and the lowest in mature rats. Thus, in old rats, the recovery of the affected structures is slower, and the recovery of detoxification systems is prolonged.

At the same time, the dynamics of the accumulation of the aromatic fraction of MMM_{280} in the blood serum indicates that the level of dysmetabolic disorders in internal organs due to CST in all age groups gradually increases from day 1 of the experiment. After 3 days, the index dominates in old rats, then in sexual mature and immature rats. In sexual immature rats, the maximum increase in the value of the studied index falls on day 14, in sexual mature rats – on days 14-21, in old rats – on day 21. By day 28, the index decreases in rats of all age

groups, but does not reach the control level. After 21 and 28 days, the index became significantly higher in old rats compared to immature rats. Thus, the intensity of dysmetabolic disorders that occurred at the systemic level is significantly higher in old rats, mainly during the period of late manifestations of traumatic disease.

Thus, local destructive processes of the brain, soft tissues, and bones as a source of endotoxins dominate in immature rats during the acute period (after 1 day) and the period of early manifestations of traumatic injury (after 7 and 14 days), and in old rats during the period of late manifestations of traumatic injury (21-28 days). At the same time, the maximum development of dysmetabolic disorders of internal organs as a source of endotoxins under conditions of CST occurs mainly in old rats and occurs during the period of late manifestations of traumatic disease. The revealed peculiarities of endotoxin accumulation in the dynamics of CST in rats of different ages indicate the high informativeness of the study of MMM fractions for understanding the mechanisms of development of endogenous intoxication syndrome in the age aspect and allow a pathogenetic approach to the choice of correction agents.

CONCLUSIONS

1. The modeling of CST in rats of different age groups is accompanied by the development of endogenous intoxication syndrome, the manifestation of which is the accumulation of MMM_{254} and MMM_{280} fractions in the blood serum, the content of which gradually increases by day 14 of the posttraumatic period, followed by a decrease by day 28 and at all times statistically significantly exceeds the control level.
2. The content of the serum fraction of MMM_{254} in immature rats in the dynamics of experimental CST statistically significantly exceeds other age groups in the acute period (after 1 day) and the period of early manifestations of traumatic illness (after 7 and 14 days). In the period of late manifestations of traumatic illness (21-28 days), the content of serum fractions of MMM_{254} and MMM_{280} significantly exceeds other age groups in old rats.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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