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THE ROLE OF OVARIECTOMY IN THE FORMATION OF ENDOGENOUS INTOXICATION SYNDROME IN THE LATE PERIOD OF AFTERSKELETAL AND COMBINED CRANOSKELETAL INJURY IN EXPERIMENT

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Summary

Causing combined traumatic brain injury in conditions of gonads removal is accompanied by increasing level of endogenous intoxication, manifested by the accumulation of fractions MSM₂₅₄ and MSM₂₈₀ in blood within two months of post-traumatic period and is significantly higher than in animals with skeletal trauma and injured animals without ovariectomy. This result demonstrates the important role of estrogens in the formation of endogenous intoxication syndrome in the conditions of mechanical injury.

Keywords: ovariectomy, cranoskeletal injury, endogenous intoxication.

Introduction. Endotoxemia plays one of the key roles in the pathogenesis of severe injury. The accumulation of endotoxins is caused by the direct lesion of tissues, disfunction of excretion organs and systemic response of the body to the accumulation of inflammatory mediators [11]. Its main mechanisms are metabolic disorders with the accumulation of

underoxidized products, increased cytolytic processes, coming out of proteolytic enzymes of lysosomes to the extracellular space, closing the vicious circle and contributes even more endotoxycosis [5]. At the same time in the body there is a complex of adaptive and compensatory reactions of sanogenic nature in the body that can be seen in the dynamics of traumatic disease periods: acute response to injury, early symptoms and the late period [2].

These disorders are important in reparative osteogenesis, because the background system of the body's response against inflammation, which is manifested by increased content of reactive oxygen species, free radicals, pro-inflammatory mediators and endotoxycosis in general, the processes of remodeling the bones are not only reduced but also their destruction deepens, that is connected with stimulation of osteoclasts by proinflammatory cytokines [3]. Almost unknown is the level of endogenous intoxication in case of injury in terms of hypoestrogen osteoporosis that occurs in postmenopausal women or against removal of gonads. Estrogens are a powerful natural antioxidants and regulators of physiological functions. Their absence can not fail to affect the systemic manifestations of severe injury.

The aim of the study is to clarify the role of ovariectomy in the formation of endogenous intoxication syndrome in the late period after skeletal and combined craneoskeletal injuries in the experiment.

Materials and methods of research. The experiments have been performed on nonlinear white female rats weighing 200-220 g. The model of postmenopausal osteoporosis has been performed by surgical removal of gonads [6]. After 1 month there was modeled an isolated fracture of the hip in one group of animals and in the second one there was caused additionally a closed traumatic brain injury (TBI) of the second level of severity [4]. In the comparison group specified injuries were modeled in healthy animals. The control group consisted of intact animals and animals with osteoporosis 1 month later after removal of gonads, which were not injured.

After 1 and 2 months of posttraumatic period there were tested molecules of average weight fractions in the liver and brain tissue, determined at the length of the wave 254 nm (MSM_{254}) and 280 nm (MSM_{280}) [9], which are among the sensitive indicators of traumatic disease progress [1, 8, 10, 12].

The obtained digital material was treated in the department of systematic statistical studies SHEE "Ternopil State Medical University named after I.Ya.Horbachevskiy, Ministry of Health of Ukraine" in the software package STATISTICA ("StatSoft Inc.", USA) using the

nonparametric criteria Mann-Whitney.

Results of the study and its discussion. As it is seen in Table 1, the content of fractions MSM₂₅₄ in blood serum 1 month later after ovariectomy was increasing concerning intact animals, but the result was statistically not probable ($p>0,05$).

Causing skeletal injury 1 month later was accompanied by a significant increase in content of fractions MSM₂₅₄ in blood serum – by 82,4% ($p<0,05$). 2 months later an indicator decreased significantly concerning the previous observation period (40,3 %, $p<0,05$) and reached the level of the control group ($p>0,05$). In conditions of combined craneskeletal injury the level of endotoxemia was higher. After 1 month of post-traumatic period an indicator increased in 2,23 times ($p<0,05$) in comparison with the control group, which was also significantly higher than most animals with skeletal injury have (22,6 %, $p<0,05$). 2 months later an indicator decreased by 39,5 % concerning the previous observation period ($p<0,05$), but continued to remain significantly higher than in control (35,3 %, $p<0,05$).

Table 1 – The content of MSM₂₅₄ in blood serum (conv. units.) in the dynamics of a polytrauma in animals with hypoestrogenic osteoporosis (M±m)

Terms of experiment	Type of injury	Initial condition	The term of observation		p
			1 month	2 months	
Without osteoporosis	The skeletal injury	0,034±0,003 (n=6)	0,062±0,004* (n=6)	0,037±0,003 (n=6)	<0,05
	The skeletal injury + TBI		0,076±0,003*^ (n=6)	0,046±0,003* (n=7)	>0,05
Osteoporosis	The skeletal injury	0,043±0,004 (n=6)	0,088±0,004* (n=7)	0,050±0,004 (n=8)	<0,05
	The skeletal injury + TBI		0,094±0,003* (n=7)	0,058±0,003* (n=7)	<0,05
p ₁			>0,05	<0,05	
p ₂			<0,05	<0,05	

Notes: they are here and in the table 2:

- # – differences between the groups of animals with and without osteoporosis in the initial state are statistically probable ($p<0,05$);
- ^ – differences between the groups of animals with skeletal injury and skeletal injury combined with TBI are statistically probable ($p<0,05$);
- * – differences concerning the control group are statistically probable ($p<0,05$);
- p₁ – probability of differences of animals with skeletal injury on the background of osteoporosis and without osteoporosis is statistically possible ($p<0,05$);
- p₂ – probability of differences of animals with skeletal injury and TBI against the background of osteoporosis and without osteoporosis are statistically possible ($p<0,05$).

Causing skeletal injuries in terms of osteoporosis after 1 month of post-traumatic period was also accompanied by a statistically probable increase of fraction MSM_{254} . Equally to the control group an indicator increased in 2,04 times ($p < 0,05$), but 2 months later it was significantly decreasing (43,2 %, $p < 0,05$) and reached the level of the control group ($p > 0,05$). In conditions of combined craneoskeletal injury the regularity of dynamics MSM_{254} content in blood serum was similar: 1 month later an indicator regarding the control group statistically probably increased – in 2,19 times ($p < 0,05$), 2 months later it decreased (by 38,3 %, $p < 0,05$ concerning the preceding observation period), but remained statistically probably higher than in the control group (by 34,9 %, $p < 0,05$). Comparison of research groups with the skeletal and combined craneoskeletal injuries themselves revealed no significant differences in the content of fractions MSM_{254} in blood serum ($p > 0,05$).

Against the background of osteoporosis after 1 month of posttraumatic period the content of fraction MSM_{254} in blood serum proved to be statistically probably higher in comparison with animals without osteoporosis in conditions of combined craneoskeletal injury (by 23,7 % $p_2 < 0,05$). After 2 months of osteoporosis the significantly higher content of the studied indicator predetermined both in the conditions of skeletal and combined injuries, respectively by 35,1 % ($p_1 < 0,05$) and 26,1 % ($p_2 < 0,05$).

Thus, the content of fraction MSM_{254} in blood serum under the influence of mechanical trauma of various localization was significantly increasing after 1 month, after 2 months it was declining, but in conditions of combined craneoskeletal injury it continues to be significantly higher than in control. A similar pattern is observed after causing injury in conditions of ovariectomy, but after 1 month against the background of craneoskeletal injury and 2 months against the background of skeletal and combined injury, an indicator is statistically probably higher.

A similar situation was observed by the content of the fraction MSM_{280} (Table 2). After causing the skeletal injury 1 month later an indicator increased in comparison with the control group by 71,8 %, 2 months later it declined, reaching the level of control ($p > 0,05$). Against the background of combined craneoskeletal injury the degree of endotoxemia was higher: the content of MSM_{280} in blood serum increased after 1 month of posttraumatic period in comparison with control in 2,05 times ($p < 0,05$) and was statistically probably higher than in most animals with skeletal trauma itself (19,4 %, $p < 0,05$). 2 months later an indicator decreased, but it continued to

remain higher than in controls (28,2 %, $p < 0,05$).

Table 2 – Content of MSM₂₈₀ in blood serum (conv. units.) in the dynamics of polytrauma in animals with hypoestrogenic osteoporosis (M±m)

Terms of of the experiment	Type of injury	Initial condition	The term of observation		p
			1 month	2 months	
Without osteoporosis	The skeletal injury	0,039±0,003 (n=6)	0,067±0,003* (n=6)	0,041±0,003 (n=6)	<0,05
	The skeletal injury + TBI		0,080±0,003*^ (n=6)	0,050±0,002* (n=7)	<0,05
Osteoporosis	The skeletal injury	0,047±0,004 (n=6)	0,094±0,004* (n=7)	0,055±0,003 (n=8)	<0,05
	The skeletal injury + TBI		0,102±0,004* (n=7)	0,063±0,003* (n=7)	<0,05
p ₁			<0,05	<0,05	
p ₂			<0,05	<0,05	

In conditions of the removal of gonads on the background of the skeletal injury the content of MSM₂₈₀ in blood serum was also significantly increasing in comparison with control – in 2,0 times ($p < 0,05$) and then decreased to the level of control ($p > 0,05$). In conditions of combined craneoskeletal injury an indicator was increasing almost in the same way after 1 month – in 2,17 times ($p < 0,05$), after 2 months – it was decreasing, but did not reach the level of control and was by 34,0 % higher ($p < 0,05$).

Thus, the pattern of violations of the content of MSM₂₈₀ in blood serum was similar to that as MSM₂₅₄. An expressed endotoxicosis was observed for two months in the posttraumatic period in the animals with combined craneoskeletal injury and was significantly higher against the background of removing the gonads.

It is known that accumulation of the faction MSM₂₈₀ in blood, which includes mainly the aromatic amino acids, occurs against a background of polyorganic disfunction [7]. This points to the development of deeper metabolic disorders and the lack of body detoxication in conditions of craneoskeletal injury that occurs against a background of low content of estrogen. This assumption is confirmed by the fact that the dynamics of the faction MSM₂₅₄, which is considered to be common integral factor of the content of substances with low and medium

molecular weight (500 Da to 5000 Da), was identical to MSM₂₈₀. So, traumatic disease against a background of ovariectomy is characterized by greater polyorganic disfunction that should be taken into account in the treatment of victims in postmenopausal period.

Conclusion. After causing the combined traumatic brain injury in conditions of removing the gonads an increase in the level of endogenous intoxication is observed, which is manifested in accumulation of the fractions MSM₂₅₄ and MSM₂₈₀ in blood within two months of posttraumatic period and is significantly higher than in animals with skeletal trauma and injured animals without ovariectomy. The obtained result demonstrates the important role of estrogens in the formation of endogenous intoxication syndrome in conditions of mechanical injury.

The prospects of further research. In future it is necessary to examine the effectiveness of hormone replacement therapy in the correction of endogenous intoxication syndrome of ovarioektomal animals.

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