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THE PECULIARITIES OF ANTIOXIDANT-PROOXIDANT BALANCE OF KIDNEY'S PAPILLARY LAYER IN SKELETAL AND CRANIOCEREBRAL INJURIES AND THEIR COMBINATIONS

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Resume. Skeletal and craniocerebral injuries simulating and their combinations within the papillary layer of a kidney is leading to a significant shift of antioxidant-prooxidant ratio with prevailing Pro-oxidant mechanisms. These mechanisms are enlarging from the first to the seventh day of the posttraumatic period and significantly higher against the background of combined cranio-skeletal injuries on the 3rd and on the 7th day of post-traumatic period.

Key words: skeletal trauma, traumatic brain injury, multitrauma, kidney, lipid peroxidation, antioxidant protection

Introduction. Lipid peroxidation activation is related to one of the main pathogenesis causes of severe trauma. [4]. In polytrauma the highest quantity of lipid peroxidation products correlates with maximal intensity of an organism's systemic response to inflammation. [3]. At present it's determined that in the course of trauma LPA and antioxidant protection indices are changing in phases with periods of pathological process intensification and its subsiding. They are also

connected tightly with the whole of systemic deviations within the organism. [2, 6]. In our previous researches we showed that skeletal and craniocerebral trauma modeling and their combination cause LP secondary products' accumulation, catalase activity exhaustion, and essential shift of antioxidant-prooxidant ratio towards prooxidant mechanisms' prevalence. These mechanisms are increasing significantly within the first week of posttraumatic period and are much higher against the background of combined cranio-skeletal trauma. [9]. However the dynamics of the indices within kidneys' medullar layer hasn't been learnt yet and it may prompt in gaining valuable information of LP role in kidneys malfunction.

The purpose of the work is to realize the peculiarities of antioxidantiprooxidant state of renal medullar layer in skeletal and craniocerebral trauma and their combination.

Materials and methods. The experiments have been carried out on 104 nonlinear white female rats, their weight was 160-180 gr, they were fed with ordinary vivarium's food. All rats were divided into 4 groups: control one (8 species) those were intact animals and the three other groups. Within the 1^{st} group skeletal trauma was simulated by striking in the certain way in the area of each hip that led to closed fracture [10], within the second group closed craniocerebral trauma of medium degree has been modeled [4], within the 3^{rd} group the above traumas has been combined. All the experiments were car ried out under tiopenthal Na anesthesia. (40 $mg \cdot kg^{-1}$ weight).

The rats were taken out of the experiment under anesthesia with the help of total phlebotomy from their hearts on the 1^{st}, 3^{rd} and the 7^{th} days of posttraumatic period. The rats' kidneys were extracted quickly and at that renal medulla was separated on the special freezing table. The content of TBS active products of LPA [1] was determined within medullar homogenate as well as catalase activity [7] and antioxidant- prooxidant index was calculated: catalase / TBS active products of LPA. [8].

The data received had to be analyzed statistically. The validity of differences

between experimental groups was evaluated with the help of special program STATISTICA 10.0 (“StatSoft, Inc.”, USA).

The results of researches and their discussion. As we can see from Table 1 under the influence of skeletal trauma in comparison with control group one can mention gradual increase TBS active products of LPA in medullar layer of kidney in an hour– 40,03 % ($p<0,001$), in 3 days – 49,49 % ($p<0,001$), in a week – 51,32% ($p<0,001$). The similar deviation was registered also after craniocerebral trauma: correspondingly 45,39, 56,79 and 69,55 % ($p<0,001$). After polytrauma content deviation TBS active products of LPA in renal medullar layer were more distinguished: in an hour the index has been increased 62,26 %, in 3 days – 78,66 %, in a week – 87,78 % ($p<0,001$).

Table 1 **– The dynamics of TBS active products of LPA in renal medullar layer content after skeletal and craniocerebral traumas and polytraumas (M±m)**

The kind of injury	Control	The duration of posttraumatic period		
		The 1st day	The 3rd day	The 7th day
Skeletal	1,097± 0,006 (n=8)	1,540± 0,009*** (n=10)	1,640± 0,026*** (n=10)	1,660± 0,026*** (n=9)
Craniocerebral		1,595± 0,010*** (n=10)	1,720± 0,023*** (n=8)	1,860± 0,029*** (n=7)
Multitrauma		1,780± 0,012*** (n=10)	1,960± 0,025*** (n=7)	2,060± 0,031*** (n=7)
p_{1-2}		<0,001	<0,05	<0,001
p_{1-3}		<0,001	<0,001	<0,001
p_{2-3}		<0,001	<0,001	<0,001

Remarks. Here and in tables 2 and 3:

1. * – verification of differences as to control group (* – p<0,05; ** – p<0,01; *** – p<0,001);

2. p_{1-2} – verification of differences of the index between groups of rats with skeletal and craniocerebral traumas; p_{1-3} – between skeletal trauma and multitrauma; p_{2-3} – between craniocerebral and polytrauma.

Comparing content of TBS active products of LPA in renal medullar layer at investigating groups by the terms of observation the following was concluded- in craniocerebral trauma in a day after craniocerebral черепно-мозковій травмі trauma one could register reliable increase the content of TBS active products of LPA in renal medullar layer if to compare with skeletal trauma (p_{1-2}<0,001). In a group with polytrauma the index under study was authentically larger in comparison with skeletal trauma itself (15,9 %, p_{1-3}<0,001) and also authentically larger if to compare with craniocerebral trauma (11,6 %, p_{2-3}<0,001). In 3 days the content of TBS active products of LPA in renal medullar layer after craniocerebral trauma was also revealed statistically authentically larger than after skeletal itself (p_{1-2}<0,05), and after polytrauma- much larger than in craniocerebral and skeletal ones (accordingly 19,5 і 13,9 %; p_{1-3}<0,001, p_{2-3}<0,001). In a week the value of index in study went on to be the largest after craniocerebral and polytraumas that turned out to be statistically authentically larger than after skeletal trauma itself (accordingly 18,23 %, p_{1-2}<0,001 and 36,46 %, p_{1-3}<0,001). As it was in previous terms of observation the index surpassed substantially the similar one in craniocerebral trauma itself (10,8 %, p_{2-3}<0,001).

As we can see from Table 2 catalase activity in medullar layer of kidney under the influence of skeletal trauma during the 1st, 3rd and 7th days of observation was proved to be statistically authentically lower than in a control groups. In a day it was lower than in control 26,4 % (p<0,001), in 3 days – 34,6 % (p<0,001). In 7 days of observation we could see essential decrease of index in study comparing with control group 40,2 % (p<0,001). The catalase activity was revealed similarly

decreased from the 1st to the 7th day in medullar layer of kidney and after polytrauma. In a day it was smaller than control 35,2 % ($p<0,001$), in 3 days – 46,4 % ($p<0,001$). After 7 days of observation one could register essential decrease of index in study comparing with control group 50,2 % ($p<0,001$). The same changes of index in study occurred against the background of polytrauma. In a day as to control group it was smaller than in control 36,2 % ($p<0,001$). In further the index lowered and in 3 days it was lower than its level in control group 56,8 % ($p<0,001$), and in 7 days essential lowering of index in study comparing with control group was revealed 60,2% ($p<0,001$).

Comparing catalase activity in renal medullar layer within studying groups by the terms of observation it turned out that on the1st day of posttraumatic period we could register statistically authentically lower catalase activity in groups o animals where craniocerebral and polytrauma were simulated comparing with skeletal trauma itself ($p_{1-2}<0,05$, $p_{1-3}<0,05$). In 3 days against the background of polytrauma the index was essentially lower than after skeletal and craniocerebral traumas (correspondingly 33,8 %, p1-3<0,001 and 19,3 %, $p_{2-3}<0,01$). In 7 days the regularity was preserved: against the background of polytrauma catalase activity of renal medullar layer was 33,6 % lower than in skeletal ($p_{1-3}<0,001$ and 20,2 % – than in craniocerebral ($p_{2-3}<0,001$).

Table 2 – **The dynamics of catalase activity in renal medullar layer after skeletal and craniocerebral traumas and after their combination (M±m)**

The kind of trauma	Control	The duration of posttraumatic period		
		The 1st day	The 3rd day	The 7th day
Skeletal	0,358± 0,008 (n=8)	0,263± 0,008*** (n=10)	0,234± 0,008*** (n=10)	0,214± 0,008*** (n=9)
Craniocerebral		0,232± 0,008*** (n=10)	0,192± 0,008*** (n=8)	0,178± 0,007*** (n=7)

Polytrauma		0,228± 0,010*** (n=10)	0,155± 0,007*** (n=7)	0,142± 0,005*** (n=7)
p_{1-2}		<0,05	<0,01	<0,01
p_{1-3}		<0,05	<0,001	<0,001
p_{2-3}		>0,05	<0,01	<0,001

As follows from Table 3 API activity in renal medullar layer under the influence of skeletal trauma turned out to be authentically lower than in control group during the 1st, the 3rd and the 7th days of observation. In a day it was lower than control 47,55 % ($p<0,001$), in 3 days – 56,14 % ($p<0,001$). In 7 days of observation we could register essential decrease of index in study comparing with control group 60,43 % ($p<0,001$). Similarly API activity in renal medullar layer was decreased from the 1st to the 7th days after craniocerebral trauma. In a day it was less than in control 55,22 % ($p<0,001$), in 3 days – 65,65 % ($p<0,001$). In 7 days of observation it was registered essential decrease of index in study comparing with control group 70,56 % ($p<0,001$). The same changes of index in study took place against the background of multitrauma. In a day as to control group it was less than control 60,74 % ($p<0,001$). In further the index went on decreasing and in a 3 days it was lower from the control group level 75,77 % ($p<0,001$), and in 7 days essential decrease of index in study was registered comparing with control group 78,84% ($p<0,001$).

Comparing API activity in renal medullar layer in investigating groups by the terms of observation it turned out that in all terms the quantity of index in study was statistically trustworthy loer within the group with polytrauma than within those with skeletal or craniocerebral ($p_{1-3}<0,001$, $p_{2-3}<0,05$-$0,001$). At that catalase activity against the background of craniocerebral trauma was essentially lower than in skeletal one ($p_{1-2}<0,01$-$0,001$).

Table3. **– The dynamics API activity in renal medullar layer after skeletal and craniocerebral traumas and their combination (M±m)**

Kind of trauma	Control	Duration of posttraumatic period		
		The 1st day	The 3rd day	The 7th day
Skeletal	0,326± 0,008 (n=8)	0,171± 0,005*** (n=10)	0,143± 0,004*** (n=10)	0,129± 0,005*** (n=9)
Craniocerebral		0,146± 0,005*** (n=10)	0,112± 0,005*** (n=8)	0,096± 0,004*** (n=7)
Polytrauma		0,128± 0,006*** (n=10)	0,079± 0,004*** (n=7)	0,069± 0,003*** (n=7)
p_{1-2}		<0,01	<0,001	<0,001
p_{1-3}		<0,001	<0,001	<0,001
p_{2-3}		<0,05	<0,001	<0,001

Thus, modeling skeletal, craniocerebral traumas and their combination is followed by TBS active products of LPA increase, decrease of catalase activity and the value of API in real medullar layer during 7 days of observation. In all terms of observation deviation of indices in study turned out essentially larger after polytrauma, second best- were after craniocerebral and the least were in skeletal trauma.

Now then, in the course of experiments carried out one could mention continual enlargement of peroxidant mechanisms. Violation of microcirculation, tissue hypoxia, 'respiratory explosion' of neutrophils and macrophages underlie these mechanisms. [4]. Against such a background active forms of oxygen accumulate which strengthen forming inflammatory mediators, deepen systemic response of organism against inflammation. Violation deepening against the background of craniocerebral and multytraumas testify to the fact that damage of

neurohormonal regulatory mechanisms play important role in pathogenesis of traumatic disease. [5].

Thus, the experiments showed that in skeletal and craniocerebral traumas lipid peroxidation processes and an exhaustion of antioxidant protection play very important role in renal malfunction. The abovementioned processes increase in renal medullar layer from the 1st to the 7th days and essentially higher on the condition of polytrauma.

Conclusion. Simulating Моделювання скелетної, черепно-мозкової травм і їх поєднаннякeletal, craniocerebral traumas and their combination in renal medullar layer leads to accumulation of lipid peroxidation secondary products, the exhaustion of catalase activity, essential shift of API towards peroxidant mechanisms increase which grow on from the 1st to the 7th days of posttraumatic period essentially higher against the background of combined cranioskeletal trauma.

The prospective of further investigations. In perspective to establish practically the effectiveness of antioxidants in correction of violations manifested within renal medullar layer in the dynamics of severe trauma.

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