

© The Author (s) 2013;

This article is published with open access at Licensee Open Journal Systems of Radom University in Radom, Poland

Open Access

This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

This is an open access article licensed under the terms of the Creative Commons Attribution Non Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

Conflict of interest: None declared. Received: 15.07.2013. Revised: 12.11.2013. Accepted: 14.11.2013.

UDC 616.36-099:546.56-008.1-06:616-001.1

**EFFECT OF SALTS OF COPPER AND ZINC ON DYNAMICS
CYTOLYTIC PROCESS IN MECHANICAL TRAUMA VARYING
SEVERITY**

Kopach O. E., Gudyma A. A.

**SHEE “I. Ya Horbachevsky Ternopil State Medical Ministry
of Public Health of Ukraine”**

Summary. In experiments on rats showed that chronic toxicity of copper and zinc salts against skeletal injuries of varying severity significantly enhances cytolysis phenomenon that manifests increased activity of aspartataminotransferase serum after 3 days of post-traumatic period. However, under these conditions occurs 3-7 days via decreased activity of alanine aminotransferase, indicating a violation of the functional state of the liver.

Key words: polytrauma, liver cytolysis, chronic intoxication, copper and zinc.

Introduction. Injuries belongs to Current's challenges. In its structure every year come from the trauma that accompanied the development of traumatic disease and is characterized by considerable disability and mortality. [9] The main cause of death of the injured body is the development of multiple organ failure. [11] One of the reasons for its occurrence is membranopatiya system caused by activation of lipid peroxidation with subsequent cell death's ID in lysosomal enzymes in this process enhances the development of systemic inflammatory reaction in the body [4].

In some works are dynamic processes cytolysis after experimental trauma, characterized phase flow with a period of growth after 3-7days, temporary prosperity – in 14 days with subsequent aggravation – in 21 days and partial restoration – in 28 days [8]. In the acute period of cranio-skeletal injuries showed phenomena growth of cytolysis within 12 hours with their decrease – after one day [3].

With the global environmental crisis in the body gets an excessive amount of heavy metals. [10] However, the processes in cytolysis of excessive intake of trauma against insufficiently studied. It can be assumed that the accumulation of heavy metals may modify the pathogenic mechanisms of trauma that requires special study.

The research was aimed at determining enzyme activity cytolysis alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the dynamics of experimental trauma against toxicity of copper and zinc salts.

Research material and methods. Experiments were performed at 150 nonlinear white male rats weighing 180-200 g. Chronic toxicity of copper sulfate and zinc was performed by daily administration into the stomach through a tube of solution at a dose of $5 \text{ mg} \cdot \text{kg}^{-1}$ of metal in terms once daily [6]. After 14 days under thiopental sodium anesthesia ($40 \text{ mg} \cdot \text{kg}^{-1}$ body weight) in the first experimental group of animals (72 individuals) modeled skeletal injury of varying severity: mild – a hip fracture, moderate – in addition cause bleeding from the femoral vein (20-22 % blood volume), which was introduced in the perirenal tissue

to form a hematoma, severe injury – additional adjacent broken hip [1]. In the second experimental group (72 individuals) modeled skeletal injury without poisoning by salts of heavy metals. Checklists were intact animals (6 individuals). Animals were taken out of the experiment under thiopental sodium anesthesia ($60 \text{ mg} \cdot \text{kg}^{-1}$ body weight) at 1, 3 and 7 days post-traumatic period by the total blood from the heart. In serum of experimental animals was determined activity of AST and ALT standardized method for Biochemical Humalyzer 2000.

These data are subject to statistical analysis. Significance of differences between experimental and control groups was assessed using the program STATISTICA 10.0 (“StatSoft, Inc.”, USA).

Research results and discussion. As can be seen from the table 1 in skeletal injuries of varying severity was marked a significant increase in serum AST activity throughout the observation period. In mild trauma, the figure in 1 day increased by 67,9 % ($p < 0,001$) in 3 days – in 2,0 times ($p < 0,001$) after 7 days – 2,5 times ($p < 0,001$). Similarly, increased AST activity after poisoning by salts of copper and zinc. In this case, after 3 days the value of the studied parameters of poisoned animals was statistically significantly greater than in not poisoned ($p < 0,05$).

Table 1. Dynamics of serum aspartate aminotransferase activity in skeletal injuries of varying severity against intoxication copper and zinc salts ($M \pm m$)

Injury	Intok-sykatsiya	Period after injury		
		1 day	3 days	7 days
Control = $(90,88 \pm 3,77) \text{ Un} \cdot \text{L}^{-1}$ (n = 6)				
Mild	No	$152,6 \pm 4,9^{***}$ (n = 6)	$182,5 \pm 4,4^{***}$ (n = 6)	$230,8 \pm 3,5^{**}$ (n = 6)
	Salts of copper and zinc	$148,7 \pm 5,6^{***}$ (n = 6)	$198,1 \pm 4,0^{***}$ (n = 6)	$234,2 \pm 4,6^{***}$ (n = 6)
p		>0,05	<0,05	>0,05
Mid-level	No	$178,1 \pm 6,6^{***}$ (n = 7)	$242,6 \pm 3,6^{***}$ (n = 7)	$274,1 \pm 6,7^{***}$ (n = 6)

	Salts of copper and zinc	203,8 ± 9,1 *** (n = 6)	266,0 ± 4,0 *** (n = 5)	272,9 ± 3,5 *** (n = 5)
p		<0,05	<0,01	>0,05
Severe	No	217,0 ± 7,6 *** (n = 8)	290,8 ± 5,0 *** (n = 8)	343,7 ± 2,7 *** (n = 8)
	Salts of copper and zinc	239,2 ± 6,9 *** (n = 7)	322,6 ± 5,5 *** (n = 7)	338,6 ± 3,8 *** (n = 6)
p		<0,05	<0,001	>0,05

Remarks:

1. * – Significance of differences in relation to the control group (* – $p < 0,05$; ** – $p < 0,01$; *** – $p < 0,001$).

2. p – significance of differences between groups of animals with chronic intoxication with salts of copper and zinc in not poisoned animals.

After an injury of moderate severity serum AST activity in relation to the control group at 1, 3 and 7 days post traumatic period was higher by 2,4, 2,7 and 3,0 times ($p < 0,001$). Last poisoning by salts of copper and zinc resulted in significantly higher levels of the studied parameters at 1 and 3 days after injury: respectively 14,4 % ($p < 0,05$) and 9,6 % ($p < 0,01$). After 7 days it reached the level not poisoned animals ($p > 0,05$).

After severe trauma serum AST activity higher than control after 1 day in 2,2 times ($p < 0,001$) in 3 days – by 2,9 times ($p < 0,001$) after 7 days – 3,8 times ($p < 0,001$). Intoxication salts of copper and zinc in these experimental conditions caused an increase in AST activity after 1 and 3 days post-traumatic period: respectively 10,2 % ($p < 0,05$) and 10,9 % ($p < 0,001$).

Serum ALT activity also increased after skeletal injuries of varying severity (Table 2). In a mild injury at 1 day post-traumatic period, this figure increased by 37,0 % ($p < 0,001$) in 3 days – by 71,3 % ($p < 0,001$) after 7 days – it fell on the preliminary observation period for 17,0 % ($p < 0,001$), but remained elevated compared to controls by 42,1 % ($p < 0,001$).

In animals poisoned skeletal injury severity too mild effects included increased activity of serum ALT during the study period of post-traumatic period, but only after 3 days the value of this index was statistically significantly higher compared with group not poisoned animals (22,2 %, $p < 0,001$).

After an injury of moderate severity serum ALT activity in the dynamics of post-traumatic period increased, respectively, in 2,0, 2,2 and 2,4 times ($p < 0,001$). Intoxication in terms of copper and zinc salts of the value of this index also increased, but after 3 it was statistically significantly lower than in not poisoned animals (13,8 %, $p < 0,05$) and after 7 days – reached level not poisoned animals ($p > 0,05$).

In severe trauma serum ALT activity in the dynamics post-traumatic period to the control group also increased: in 1 day – 2,3 times in 3 days – by 2,5 times in 7 days – 2,9 times ($p < 0,001$). After poisoning by salts of copper and zinc in 1 day post-traumatic period activity of ALT serum levels exceeded in not poisoned animals by 25,4 % ($p < 0,001$) after 3 days stood at not poisoned animals but after 7 days became statistically significantly lower – 9,0 % ($p < 0,001$).

Table 2. Dynamics of serum alanine aminotransferase activity in skeletal injuries of varying severity against intoxication copper and zinc salts ($M \pm m$)

Injury	intoxication	Period after injury		
		1 day	3 days	7 days
Controls = $(76,00 \pm 5,30) \text{ Un} \cdot \text{L}^{-1}$ (n = 6)				
Mild	No	$104,1 \pm 4,8^{***}$ (n = 6)	$130,2 \pm 3,5^{***}$ (n = 6)	$108,0 \pm 3,2^{***}$ (n = 6)
	Salts of copper and zinc	$108,2 \pm 4,2^{***}$ (n = 6)	$159,1 \pm 3,6^{***}$ (n = 6)	$111,9 \pm 3,5^{***}$ (n = 6)
p		$>0,05$	$<0,001$	$>0,05$
Mid-level	No	$142,3 \pm 4,0^{***}$ (n = 7)	$170,8 \pm 3,3^{***}$ (n = 7)	$193,1 \pm 5,3^{***}$ (n = 6)
	Salts of copper and zinc	$150,6 \pm 5,2^{***}$ (n = 6)	$147,3 \pm 3,7^{***}$ (n = 5)	$188,1 \pm 4,6^{***}$ (n = 5)

p		>0,05	<0,0 5	>0,05
Severe	No	174,3 ± 5,1 *** (n = 8)	193,1 ± 5,3 *** (n = 8)	220,8 ± 7,0 *** (n = 8)
	Salts of copper and zinc	218,5 ± 9,9 *** (n = 7)	188,1 ± 4,6 *** (n = 7)	178,7 ± 4,5 *** (n = 6)
p		<0,0 1	>0,05	<0,001

The results indicate that skeletal injuries of varying severity significantly affects local and systemic manifestations of her body's reaction to trauma, manifested a significant increase in the activity of marker enzymes AST and ALT cytolysis. In this case increasing severity of the injury the activity of these enzymes in serum increases. as this process increases from the first to the seventh day post-traumatic period. These findings support the current understanding of the pathogenesis of severe trauma is described in several publications [5, 2].

Previous toxicity of copper and zinc salts leads to a greater increase in activity of AST in minor injuries – after 3 days, and trauma moderate and severe - alternation 1 and 3 days. At excessive flow of salt stimulates the processes of cytolysis. This can occur indirectly through increased lipid peroxidation, as shown in the works of some authors [12].

In turn, the response of serum ALT influenced toxicity of copper and zinc salts has its own characteristics. If the injury mild its dynamics was similar as AST, the trauma medium through 3 days of post-traumatic period, the value of this index was significantly lower than in not poisoned animals, and in severe injury from the first to the seventh day activity of this enzyme also decreased after 7 days was significantly lower than in animals that heavy metals are not injected. These results suggest that animals arose violation of the functional state of the liver associated with both toxic effects studied mixtures of heavy metals, and each of them in particular. A similar decrease in enzyme activity in liver poisoning by salts of heavy metals was celebrated in [7].

So , severe skeletal injury against excessive flow of salts of copper and zinc followed by the cytolytic syndrome, but with increasing injury potentiates the toxic

effects of violation of the functional state of the liver, accompanied by a decrease in serum ALT concentrations in post-traumatic period.

Conclusions. 1. Mechanical injuries of varying severity followed by the cytolytic syndrome, which manifests itself increase the activity of alanine and aspartate aminotransferase serum from the first to the seventh day post-traumatic period.

2. Excessive flow of salts of copper and zinc enhances cytolysis phenomena, manifested an increase in serum aspartate aminotransferase activity especially after 3 days of post-traumatic period, regardless of the severity of the injury.

3. Amid toxicity of copper and zinc salts moderate injury and severe injury is accompanied by decreased activity of alanine aminotransferase about non-poisonous animals under three and seven days of the experiment, indicating increased liver dysfunction in pathological gene's action factors of intoxication and trauma.

In the future provides a systemic study of the variation of organism in toxicity of copper and zinc salts and skeletal injuries of varying severity to develop a pathogenesis based methods of correction.

References

1. Volotovska N.V. Features apoptosis of hepatic macrophages under the influence of mechanical injuries of varying severity in rats / N.V. Volotovska, A.A. Hudyma // Clinical and Experimental Pathology. - 2012. - T 11, № 3 (41), Part 1. - P. 24-26.

2. Volotovska N.V. Features reaction of lipid peroxidation, antioxidant, endogenous intoxication and cytolysis under the influence injuries of varying severity / N.V. Volotovska, A.A. Hudyma // achievements of Clinical and Experimental Medicine. - 2012. - № 1 (16). - S. 29-33.

3. Goshenko A.I. Dynamics proteins forming function liver and processes in cytolysis during the acute response to combined cranio-skeletal injury / A. I.

Goshenko, R.M. Boris, A. A. Hudyma // Bukovina Medical Journal. - 2013. - T. 17, № 2 (66). - S. 29-33.

4. Dziuba D.A. Indicators of activation of apoptosis during severe polytrauma / D.A. Dziuba, J. R. Malys, L. Zhrzheblivskaya // Ukrainian Journal of extreme medicine named G.O. Mozhaeva. - 2008. -T. 9, № 1. - S. 53-58.

5. Yelskiy V.N. Modeling cranio-skeletal injury / V. N. Yelskiy, S.V.Zyablytsev - Donetsk: Publishing House "New World", 2008.- 140 p.

6. Zasyekin D. Use of laboratory rats to create biological object with a high content of heavy metals / D.A. Zasyekin, I. Kalinin // Science. Journal of NAU. - 1999. - Issue. 19. - S. 21-24.

7. Zasyekin D.A. The development of the pathological process in animals under conditions of intoxication body by heavymetals salts // Science. herald NAU. - 2001. - Vol. 42.-S. 90-95.

8. Kozak D. Dynamics of cytolysis in trauma / D.V. Kozak // Hospital Surgery. - 2012. - № 2. - S. 50-52

9. Providing medical assistance to victims of polytrauma on the hospital stage: guidelines / G.G Roschin, Y. Gaydayev, A.V. Mazurenko [et al.]. -, 2003. - 33 p.

10. Environmental Monitoring Program Ternopil region in 2006 - 2010. - Ternopil, 2005. - 22 p.

11. Seleznev S. Changes of Internal organs functions in severe mechanic injuries / S.A. Seleznev, S.F. Bahnenko, Y.B. Shapot // Dysfunction of the brain and internal organs with combined mechanical injury and terminal conditions: Materials to the "round table" / St. Petersburg. : Research Institute of Emergency Care. II Dzhanelidze. - St. Petersburg., 2001. - 18.

12. Carpenter O.B. Prooxidant-antioxidant status of the body carp at sublethal concentrations of copper (II) / O.B. Carpenter, N.G Zinkovsky, A.E. Mudra [et al.] // Scientific notes of Ternopil Pedagogical University. Series: Biology. - 2000. - № 3 (10). - S. 72-78.