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The peculiarities of the functional state of the liver under conditions of skeletal trauma, thermal burns of the skin and their combinations in the period of later manifestations of traumatic disease in the experiment

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Abstract

Aim: To find out the peculiarities of the functional state of the liver under conditions of skeletal trauma, thermal burns of the skin and their combination in the period of late manifestations of traumatic disease in the experiment.

Materials and methods. 60 non-linear white male rats weighing 180-200 g were used in the experiments. In thiopentalonate sodium (40 mg / kg-1) in the first experimental group (24 animals), a skeletal injury was simulated by applying a metered impact to each thigh, which caused their closed fracture. In the second experimental group (30 animals) simulated skin burns III A-B degree 10-11% of the surface of the body - to the depilated surface of the back was applied copper plate of 28 cm2, pre-immersed in boiling water for 3-5 minutes. In the third experimental group (30 animals), the two lesions were combined. The control group was a group of intact animals (6 animals).

After 14, 21, and 28 days after injury in thiopental-sodium (60 mg • kg-1 mass) conditions, in 6 animals of each experimental group studied the bile-forming function of the liver by catheterization of the common bile duct and bile intake for 1 hour. In the obtained

bile was determined by the concentration of total bile acids, cholesterol, conjugated bilirubin. The cholate-cholesterol coefficient and the degree of conjugation of bilirubin were calculated. From the experiment, animals were removed after bile sampling by total bloodletting from the heart.

Results. Under the influence of simulated injuries during the late manifestations of traumatic disease, there was a violation of the bile function of the liver, as evidenced by a decrease in the concentration in the bile of total bile acids, conjugated bilirubin and the degree of its conjugation. The development of liver dysfunction depended on the type of trauma. Against the background of the skeletal injury, the indicators reached their minimum level up to 21 days and up to 28 days - they returned to normal. Under thermal burns of the skin after 14 days, the violation of the studied parameters was greater than after a skeletal injury. In the future, the indicators grew, but up to 28 days did not reach the level of control. The greatest violations were noted after applying a combined injury, starting from 21 days of the experiment. Their recovery is slower. The indicated dynamics of the content of total bile acids and cholesterol led to an increase in the lithogenic properties of bile, as evidenced by a decrease in the cholesterol-cholesterol index. The rate was the smallest up to 28 days in conditions of thermal burn of the skin and combined injury.

Conclusion. In the period of late manifestations of traumatic disease, there is a violation of the functional state of the liver, which dominates in conditions of combined trauma from 21 days does not subside until 28 days of the experiment.

Key words: skeletal trauma, thermal skin burn, combined trauma, bile-forming liver function.

Introduction. A characteristic feature of modernity is the increase in the number of industrial accidents and disasters, local armed conflicts and terrorist attacks, which lead to an increase in the number of victims with severe multiple and combined injuries. [8]. In Ukraine, more than 4.5 million people suffer injuries of varying severity each year [10]. Mortality due to injuries in recent years has a steady upward trend and concerns mainly the most able-bodied population of Ukraine under the age of 40 years.

In modern wars, combat pathology differs in a variety of forms [1, 11]. Due to the effects of the fire of fires, incendiary mixtures in combination with mechanical injuries caused by a shock wave (mine explosive wounds) or various damaging elements (bullets, fragments), combined thermo-mechanical lesions arise, which are characterized by significant severity

and high mortality. An important feature of combined injury is the development of a mutual burden syndrome, in which the pathological process caused by each of the damaging factors is more difficult than conventional monofactorial lesions. A complex optic traumatic shock develops. Bleeding from damaged tissues and organs, plasma and lymphatic waste of injured and burnt tissues cause hypovolemia, hemodynamic disturbances and oxygen transport. A decrease in the blood supply to tissues and organs as a result of hypotension contributes to an increase in hypoxia, the occurrence of acidosis, and the appearance of toxic substances in the blood. All this causes a violation of the functions of organs remote from the place of direct damage. [5]. It is the development of multiple organ failure that becomes the main cause of death of the body after a combined injury during both early and late manifestations of a traumatic disease that requires in-depth study.

Objective: to find out the features of the functional state of the liver under conditions of skeletal trauma, thermal burns of the skin and their combination during the late manifestations of traumatic disease in the experiment.

Materials and methods. 60 non-linear white male rats weighing 180-200 g were used in the experiments. Under conditions of thiopental salmon anesthesia (40 mg kg – 1) in the first experimental group (24 animals), a skeletal injury was simulated by delivering a metered blow to each thigh that caused their closed fracture [9]. In the second experimental group (30 animals), a skin burn of type III AB was simulated to a degree of 10-11% of the body surface; a copper plate with an area of 28 cm2, previously immersed in boiling water for 3-5 minutes, was applied to the depilated surface of the back skin. In the third experimental group (30 animals), the two lesions were combined. The control group was a group of intact animals (6 animals).

14, 21 and 28 days after injuries under conditions of thiopental sodium anesthesia (60 mg • kg -1 mass), the liver function was studied in 6 animals of each research group by catheterization of the common bile duct and sampling of bile for 1 hour. In the obtained bile, in accordance with the recommendations [4], the concentration of total bile acids and cholesterol was determined. Also in bile, the concentration of conjugated bilirubin was determined by the van den Berg method in the modification of M.P. Skakun. The cholate-cholesterol coefficient (total bile acids / cholesterol) and the degree of conjugation of bilirubin (conjugation of bilirubin 100 / total bilirubin) were calculated. From the experiment, the animals were removed after the collection of bile by the method of total bloodletting from the heart.

All experiments were carried out in accordance with the general rules and provisions of

the European Convention for the Protection of Vertebrate Animals used for research and other scientific purposes (Strasbourg, 1986), the General Ethical Principles of Animal Experiments (Kiev, 2001), and the Law of Ukraine “On the Protection of Animals from ill-treatment "(2006), as well as according to the" Scientific and practical recommendations on the maintenance of laboratory animals and work with them. "

The significance of the differences between the experimental groups was evaluated using the nonparametric Mann-Whitney test.

Results and its discussion. As can be seen from the table. 1, the content in the bile of total bile acids against a skeletal injury after 14 days was significantly less than in the control (by 31.5%, $p<0,05$), and continued to decrease up to 21 days (by 17.2% compared with the previous observation period ($p<0,05$).

Table 1 - The content of total bile acids in bile (g l-1) after skeletal injury, thermal burns of the skin and their combination (M±m)

Type of injury	Control	Duration of the post-traumatic period		
		14 day	21 day	28 day
Skeletal	2,54±0,09 (n=6)	1,74±0,10* (n=8)	1,44±0,08*14 (n=10)	2,28±0,10^{14,21} (n=9)
Thermal burns skin		1,41±0,07* (n=7)	1,58±0,06* (n=9)	2,00±0,07*^{14,21} (n=8)
Combined		1,58±0,06* (n=6)	1,28±0,06* (n=7)	1,66±0,07*^{21} (n=6)
p_{1-2}		<0,05	>0,05	>0,05
p_{1-3}		>0,05	>0,05	<0,05
p_{2-3}		>0,05	<0,05	<0,05

Notes. Here and in other tables:

1. * – the differences in the control group were statistically significant ($p<0,05$);

2. ^{14,21} – differences between 14 and 21 days, respectively, are statistically significant ($p<0,05$);

p_{1-2} – the significance of differences between groups of animals with skeletal injury and thermal burns of the skin; p_{1-3} – between skeletal trauma and combined trauma; p_{2-3} – between thermal skin burns and combined injuries.

After 28 days the indicator increased and reached the level of the control group ($p>0,05$). Under thermal burns of the skin, the content of total bile acids in bile gradually increased from 14 to 28 days, however, at all observation times it was significantly less than

in the control (in accordance 44,5, 37,8 i 21,2 %, $p<0,05$). After modeling the combined injury, the indicator was also significantly lower at all times than in the control (in accordance 37,8, 49,6 i 34,6 %, $p<0,05$). A characteristic feature of its dynamics was a decrease to 21 days, followed by a significant increase after 28 days (on 29,7 % compared to the previous observation period, $p<0,05$).

A comparison of the research groups showed that after 14 days the total bile acid content in bile was statistically significantly lower in the group in which the thermal burn of the skin was simulated compared to the skeletal injury (on 19,0 %, $p_{1-2}<0,05$). However, starting from 21 days, the indicator became significantly less in the group with combined trauma. After 21 days in this group, the indicator was 18.9% less than in animals with thermal skin burn ($p_{2-3}<0,05$); after 28 days - 27.1% less than in animals with skeletal trauma ($_{p1-3}<0,05$) and 17.0% than in animals with thermal skin burns ($p_{2-3}<0,05$).

The bile content of cholesterol (Table 2) in animals that simulated a skeletal injury, during the late manifestations of traumatic disease, practically did not undergo significant changes compared to the control group ($p>0,05$). A similar situation was observed in animals that simulated thermal skin burns ($p>0,05$ compared to control). However, in the group of animals to which combined trauma was simulated, the rate decreased to 21 days, which was statistically significantly lower compared to the control (21,7 %, $p<0,05$) and compared to the previous observation period (25,0 %, $p<0,05$). In the future, up to 28 days, the indicator grew and did not differ significantly from the control group ($p>0,05$).

Table 2 - Cholesterol content in bile (hl-1) after skeletal injury, thermal burn of the skin, and combinations (M±m)

Type of injury	Control	Duration of the post-traumatic period		
		14 day	21 day	28 day
Skeletal	0,23±0,02 (n=6)	0,21±0,01 (n=8)	0,25±0,02 (n=10)	0,24±0,01 (n=9)
Thermal burns skin		0,21±0,01 (n=7)	0,22±0,01 (n=9)	0,25±0,01 (n=8)
Combined		0,24±0,01 (n=6)	0,18±0,01*14 (n=7)	0,21±0,01 (n=6)
p_{1-2}		>0,05	>0,05	>0,05
p_{1-3}		>0,05	<0,05	>0,05
p_{2-3}		>0,05	<0,05	<0,05

Comparing the study groups by observation time, we found that after 14 and 28 days there were no statistically significant differences between the observation groups (p_{1-2}>0,05, p_{1-3}>0,05, p_{2-3}>0,05). However, after 21 days, the cholesterol content in the bile was significantly lower in the group with combined trauma than in the groups with skeletal trauma and thermal burns of the skin (in accordance 28,0 i 18,2 %, p<0,05).

The content of conjugated bilirubin in bile (Table 3) under skeletal injury after 14 and 21 days was significantly less than in the control (in accordance 20,2 i 24,9 %, p<0,05). After 28 days the indicator reached the level of the control group (p>0,05). After thermal burns of the skin, the indicator at all times was statistically significantly lower compared to the control (in accordance 29,6, 20,1 i 18,2 %, p<0,05). It is noteworthy that in this research group the indicator gradually increased and after 28 days showed substantially more than after 14 days (16,3 %, p<0,05). In the case of combined trauma, the indicator was also lower in all terms than in the control (in accordance 35,0, 39,6 i 25,0 %). In this group, the indicator reached its minimum value in 21 days and grew up to 28 days, which was statistically significant (24,2 %, p<0,05).

Table 3 - The content of conjugated bilirubin in bile (μmoll-1) after a skeletal injury, thermal burn of the skin, and combinations (M±m)

Type of injury	Control	Duration of the post-traumatic period		
		14 day	21 day	28 day
Skeletal	69,65± 3,39 (n=6)	55,58±1,92* (n=8)	52,28±2,98* (n=10)	60,52±2,74 (n=9)
Thermal burns skin		49,00±3,13* (n=7)	55,60±1,92* (n=9)	56,98±1,80*14 (n=8)
Combined		45,25±3,44* (n=6)	42,07±3,37* (n=7)	52,27±2,97*21 (n=6)
p_{1-2}		>0,05	>0,05	>0,05
p_{1-3}		<0,05	<0,05	<0,05
p_{2-3}		>0,05	<0,05	>0,05

Comparison of the research groups with each other showed that after 14 and 28 days in the group of animals that simulated a combined injury, the content in the bile of conjugated bilirubin was significantly lower compared to the group in which they caused a skeletal injury (in accordance 18,6 i 13,6 %, p_{1-3}<0,05). After 21 days, against the background of a combined injury, the indicator was statistically significantly lower than with a skeletal injury or thermal burn of the skin (in accordance 19,5 %, p_{1-3}<0,05 and 24,3 %, p_{2-3}<0,05).

Analysis of the cholesterol-cholesterol coefficient showed (Table 4), under conditions of a skeletal injury, the magnitude of the test parameter at all observation times was statistically significantly less than in the control (in accordance 26,3, 48,4 i 14,6 %, $p<0,05$). It is noteworthy that after 21 days the indicator reached its minimum and was 30.0% less than after 14 days ($p<0,05$), however, after 28 days it grew and exceeded the level of 21 days by 65.6% ($p<0,05$). After thermal burns, the index was also less than the control at all times (in accordance 37,6, 33,7 i 27,7 %, $p<0,05$). In the dynamics of the experiment, the indicator grew, but this result was not statistically likely ($p>0,05$). After modeling the combined injury, the cholesterol coefficient after 14 days was lower than the control by 40.0% ($p<0,05$), after 21 days - by 34.3% ($p<0,05$), after 28 days - by 27.9% ($p<0,05$). As you can see, in dynamics, the indicator gradually increased from 14 to 28 days, and after 28 days it was significantly greater than after 14 days (by 20,1 %, $p<0,05$).

Table 4 - cholesterol-cholesterol coefficient of bile after a skeletal injury, thermal burn of the skin and their combination (M±m)

Type of injury	Control	Duration of the post-traumatic period		
		14 day	21 day	28 day
Skeletal	11,17± 0,55 (n=6)	8,23±0,55* (n=8)	5,76±0,32*14 (n=10)	9,54±0,45*21 (n=9)
Thermal burns skin		6,97±0,59* (n=7)	7,41±0,62* (n=9)	8,08±0,51* (n=8)
Combined		6,70±0,21* (n=6)	7,34±0,58* (n=7)	8,05±0,44*14 (n=6)
p_{1-2}		>0,05	<0,05	<0,05
p_{1-3}		<0,05	<0,05	<0,05
p_{2-3}		>0,05	>0,05	>0,05

Comparing the study groups by the observation time, it was found that after 14 days the value of the cholesterol coefficient in the conditions of combined injury was statistically significantly lower than after modeling a skeletal injury (by 18,6 %, $p_{1-3}<0,05$). After 21 days, the minimum level of the indicator was noted after modeling skeletal injury compared with other research groups (in accordance 22,3 i 21,5 %, $p_{1-2}<0,05$, $p_{1-3}<0,05$). After 28 days, on the contrary, under conditions of skeletal injury, the indicator was significantly higher than in other experimental groups (in accordance 18,1 %, $p_{1-2}<0,05$ and 18,5 %, $p_{1-3}<0,05$).

As can be seen from the table. 5, the degree of conjugation of bilirubin after applying a skeletal injury after 14 and 21 days was significantly less than in the control (in accordance

14,4 і 20,0 %, $p<0,05$). After 28 days, the indicator returned to the level of control ($p>0,05$). After modeling a thermal burn of the skin, the indicator became significantly lower than in the control after 14 and 28 days (in accordance 17,8 і 13,4 %, $p<0,05$). After 21 days, it temporarily increased and did not significantly differ from the level of control ($p>0,05$). The application of combined injury was also accompanied by a decrease in the test parameter compared with the control after 14 and 21 days (in accordance 21,6 і 22,3 %, $p<0,05$). After 28 days, the indicator grew and did not statistically significantly differ from the level of control ($p>0,05$).

Table 5 - The degree of bilirubin conjugation (%) after skeletal injury, thermal burns of the skin and their combination (M±m)

Type of injury	Control	Duration of the post-traumatic period		
		14 day	21 day	28 day
Skeletal	66,18± 3,10 (n=6)	56,68±2,53* (n=8)	52,91±2,71* (n=10)	58,95±2,16 (n=9)
Thermal burns skin		54,37±4,52* (n=7)	59,98±2,16 (n=9)	57,30±2,50* (n=8)
Combined		51,90±3,33* (n=6)	51,40±2,82* (n=7)	55,97±3,81 (n=6)
p_{1-2}		>0,05	<0,05	>0,05
p_{1-3}		>0,05	>0,05	>0,05
p_{2-3}		>0,05	<0,05	>0,05

Comparison of the research groups showed that after 14 and 28 days in terms of the degree of conjugation of bilirubin, there were not significant differences between the research groups ($p_{1-2}>0,05$, $p_{1-3}>0,05$, $p_{2-3}>0,05$). However, after 21 days, the indicator was significantly less than the conditions of skeletal and combined injuries compared to a simulated thermal skin burn (in accordance 11,8 % ($p_{1-2}<0,05$) and 14,3 % ($p_{2-3}<0,05$)).

The results obtained indicate that under the influence of simulated injuries during the late manifestations of traumatic disease, there is a violation of the desirable function of the liver. This is indicated by a decrease in the concentration in the bile of total bile acids, conjugated bilirubin and the degree of its conjugation. The development of liver dysfunction depends on the type of trauma. So, against the background of the most skeletal injury, the indicators reach their minimum level up to 21 days and up to 28 days - normalize. In conditions of thermal skin burn after 14 days, the violation of the studied parameters is greater than after a skeletal injury. In the future, the indicators increase, but up to 28 days do not

reach the level of control. The greatest violations are noted after applying a combined injury, starting from 21 days of the experiment. Their recovery is slower. The results obtained are consistent with the data of our previous studies, in which it was shown that during the late manifestations of traumatic disease against the background of simulated injuries, prooxidant mechanisms dominate, the level of cytolysis and cytokinogenesis is higher, which dominate against the background of combined injury and do not reach the control level after 28 days [2, 3, 6]. It can be assumed that the revealed violations are based on the systemic effect of skeletal trauma and thermal burn, which is accompanied by destruction of cell membranes, in particular, both the endoplasmic reticulum, where bile acids are synthesized from cholesterol, and the Golgi complex, where indirect bilirubin is conjugated. Given that the pool of bile acids that are excreted with bile consists of those that are synthesized from cholesterol in the myosomal system of hepatocytes and those that return to the liver due to absorption in the intestines and are re-absorbed by the liver (enterohepatic recirculation), it can be assumed that in the mechanism of decreasing the content of bile acids, there is a decrease in the ability of the liver to capture bile acids, is a clear evidence of the development of hepatic dysfunction. In the group of animals with combined trauma, after 21 days, the cholesterol content in bile also decreases, together with a decrease in the total bile acid content, indicates a violation of the ability of the liver to capture cholesterol from the blood, transform it into bile acids and secrete into bile, and additionally indicates a violation of the functional state of the liver .

The indicated dynamics of the content of total bile acids and cholesterol led to an increase in the lithogenic properties of bile, as evidenced by a decrease in the cholesterol-cholesterol index. The rate was the smallest up to 28 days in conditions of thermal burn of the skin and combined injury.

It is noteworthy that the most skeletal injury was characterized by the phenomenon of secondary exacerbation after 21 days of the post-traumatic period. At this time, violations of the studied parameters became greater than after 14 days, however, up to 28 they returned to normal or changed towards the control group. This phenomenon, according to the literature, is a characteristic sign of skeletal severe trauma, and, according to the authors, indicates the completion of the formation of the immune response as a reaction to trauma [7, 12].

So, in the period of late manifestations of traumatic disease, there is a violation of the functional state of the liver, which dominate in the languages of combined injury and does not subside until the 28th day of the experiment. The results should be taken into account in understanding the pathogenesis of liver failure in the late post-traumatic period.

Conclusions. 1. The period of late manifestations of traumatic disease in conditions of skeletal injury, thermal burns of the skin and their combination is characterized by a significant violation of the biliary function of the liver, manifested by a decrease in the content of total bile acids in the bile, conjugated bilirubin, cholesterol, and a deterioration in the lithogenic properties of bile.

2. Violation of the studied parameters after modeling a skeletal injury reaches a maximum after 21 days and up to 28 days in most cases normalize, while after a thermal burn of the skin and combined injury continue to be significantly less compared with the control during the entire observation period.

3. The application of a combined injury after 21 days leads to the lowest content in the bile of total bile acids, cholesterol, conjugated bilirubin compared with other research groups. Up to 28 days, the indicators improve, but the content of total bile acids and cholesterol in the bile remains lower.

4. A characteristic feature of injuries of various origins is a significant decrease in the cholesterol-cholesterol coefficient, the value of which reaches the control level up to 28 days, indicating an increase in the lithogenic properties of bile. The value of the indicator after 28 days is significantly lower after a thermal burn of the skin and a combined injury.

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