EFFECT OF COMBINED THERAPY WITH INFUSION CHANGING RATES OF ENDOGENOUS INTOXICATION IN RATS IN SEVERE COMBINED TRAUMA OF THE ABDOMINAL CAVITY (experimental study).

Krylyuk V.O., Gudyma A.A.

1Ukrainian Research Center for emergency medical care and emergency medicine

2I.Ya. Horbachevsky Ternopil State Medical University

Summary. This paper studied feature of endogenous intoxication in experimental animals combined trauma of the abdomen, after which the simulation injury after 10 minutes was administered intravenously hyperosmolar solution "Refortan" and colloidal hyperosmolar solution «HAES-LX5%» 50% in the volume of lost blood. We found that in the group of animals where the replacement of blood loss was conducted colloidal solution hyperosmolar endogenous intoxication level was lower.

Keywords: severe combined trauma, endogenous intoxication, infusion therapy, experiment.

Introduction. Severe combined injury remains an issue of urgent surgery [1, 4, 9]. According to WHO each year in the world dies from injuries about 2 million people. [8] In Ukraine only mortality due to car accidents every year is about 6.7 million people. In general, the structure of causes of death in traumatic injury is a leader among men and women of working age. The largest share of these statistics takes the associated trauma, which is 60-70 % [2, 7]. Mortality in combined injuries is 40-80 % [1, 10]. Much of the
victims receive severe combined injury of the abdominal cavity.

In scientific studies, researchers suggest the need to study the characteristics of traumatic disease. Determination of the pathophysiological features of its development will help improve the results of treatment of patients. One of the central components of the pathogenesis of traumatic disease is endogenous intoxication (EI). On the one hand, it is endotoxicosis cause dysfunction of organs and systems of the majority and the formation of multiple organ failure, on the other hand, the dysfunction of vital organs (liver, kidneys, gastrointestinal tract, central nervous system, cardiovascular system) leads to inhibition detoxification process of the development of endotoxemia phenomena [3]. These changes due to the accumulation of toxic metabolic products which do not have time to put out of the body through the abundance of their formation and development of appropriate systems failure [12]. Dynamics of indicators of EI in wound traumatic period clearly depends on the severity of the injury with an increase of up to 3 days [11]. Along with the choice of an adequate surgical treatment, in patients with severe combined trauma of the abdominal cavity according to many experts, there is the issue of adequate tactics for prehospital and early hospital stages. Particularly important is the choice of tactics infusion therapy [5, 6].

Objective: To study the effect of combined infusion therapy on the development of endogenous intoxication in experimental animals combined injury of the abdominal cavity.

Materials and methods. In pubescent white rats, Wistar, weighing 200 to 220 g simulated severe combined injury of the abdominal cavity: after propofol anesthesia, the animal deposited dose kick in area abdomen with a special device (patent UA 76,875 U). Blood loss was achieved by accessing and crossing the femoral vein in a volume of 20 to 22% of circulating blood volume of the animal, followed by fracture of the femur. Delayed administration of infusion was 10 min. The animals were divided into three groups: the first experimental group (EG -1, 48 animals) not treated with infusion solutions, the second experimental group (EG -2, 48 animals) were injected intravenously hyperosmolar solution "Refortan" in volume of 50% of the lost blood, the third experimental group (EG -3, 48 animals) were injected new colloidal solution hyperosmolar «HAES-LX5%», designed to «Institute of blood Pathology and transfusion Medicine, Academy of Medical Sciences of Ukraine", 50% of the volume of blood lost. The solution was injected with a speed of 8 drops / min. The animals were examined at 1, 6, 12 and 24 h after causing injury, which corresponded to the period of acute response to injury [12]. Each treatment group consisted of 12 animals. These
values were compared with the control group (12 healthy animals), which was introduced only in anesthesia. For determination of endogenous intoxication we determined the average molecular weight (AMW$_{250}$ and AMW$_{280}$).

**Methodology for analyzing of factual research.** According to the characteristics of groups of signs for distribution, according to the law of Gauss, we determined the arithmetic mean and standard error (M ± m). In order to establish the link between distress ranging polynomial trend line to historical data reliability coefficient was calculated approximation (R2).

To assess the degree of random differences in indicators that were studied have used non-parametric analysis of variance with multiple comparisons definition of rank N-test Kruskal - Wallis test (Kruskal-Wallis test). The critical level of significance was calculated by the formula: $p = 1 - 0.95^1 / n$, where $n$ - number of comparisons, ie, $(0.05 / 3)$. When comparing the three groups of pairwise differences between groups considered statistically significant at $p < 0.017$, when comparing the four groups in pairs - $p < 0.0125$.

Statistical analysis was performed using Statistical Package «STATISTICA 8.0.» (StatSoft Inc., USA, 2007).

When working with laboratory animals followed international standards of humane treatment of animals in accordance with the rules of the "European Convention for the protection of vertebrate animals used for experimental and other scientific purposes" (European Convention, 1984), of guidelines on State Pharmacological Center MoH Ukraine "Preclinical studies of medical means." Euthanasia of rats throughout the experiment conducted by blood from the heart total after previous propofol anesthesia (60 mg / kg intravenously).

The obtained results and their discussion.

**Table 1.**

**Key performance indicator enzymes and endogenous intoxication 1 h after severe trauma (M ± m)**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Control group (n=12)</th>
<th>Experimental groups</th>
<th>Kruskal-Wallis, H-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMW$_{254}$, st. units</td>
<td>0.015±0.003</td>
<td>0.033±0.005</td>
<td>0.028±0.001</td>
</tr>
<tr>
<td>AMW$_{280}$, st. units</td>
<td>0.014±0.002</td>
<td>0.034±0.004</td>
<td>0.028±0.001</td>
</tr>
</tbody>
</table>
1 hour after receiving serious injuries in rats were observed significant differences between the indexes AMW\textsubscript{254} (H = 8.08; p = 0.018) and AMW\textsubscript{280} (H = 3.29; p = 0.193) in the study group. It shows the lack of exposure and Refortan solution HAES-LX5% on wound stage of the shock period.

Table 2.

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<tbody>
<tr>
<td>AMW\textsubscript{254}, st. units</td>
<td>0.015±0.003</td>
<td>0.143±0.009</td>
<td>0.151±0.001</td>
</tr>
<tr>
<td>AMW\textsubscript{280}, st. units</td>
<td>0.014±0.002</td>
<td>0.144±0.007</td>
<td>0.153±0.001</td>
</tr>
</tbody>
</table>

After 6 hours after receiving serious injuries in rats observed significant differences between the indexes AMW254 (H = 21.12; p <0.017) and AMW280 (H = 21.25; p <0.017) in the study group. As evidenced at the beginning of the impact and Refortan solution HAES-LX5% to reversal of shock in period.

Table 3.

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<td>0.153±0.001</td>
</tr>
</tbody>
</table>

12 hours after receiving serious injuries in rats were observed significant differences between the indexes AMW254 (H = 3.41; p = 0.183) and AMW280 (H = 9.280; p = 0.017) in the study group. It shows the lack of exposure and Refortan solution
HAES-LX5% on stage 12 of the period of shock.

### Table 4.

**Key performance indicator enzymes and endogenous toxicity at 24 h after severe trauma (M m)**

<table>
<thead>
<tr>
<th>Indicator</th>
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<th>Experimental groups</th>
<th>Kruskal-Wallis, H-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMW\textsubscript{254}, st. units</td>
<td>0.015±0.003</td>
<td>0.168±0.03</td>
<td>0.1±0.007</td>
</tr>
<tr>
<td>AMW\textsubscript{280}, st. units</td>
<td>0.014±0.002</td>
<td>0.18±0.03</td>
<td>0.101±0.004</td>
</tr>
</tbody>
</table>

Within 24 hours after receiving serious injuries in rats observed significant differences between the indexes AMW254 (H = 10.51; p <0.017) and AMW280 (H = 18.93; p <0.017) in the study group. It shows the bar, but the heterogeneous impact Refortan and HAES solution to reversal of shock in period 24 hours after injury.

![Image](pic1.png)

**Pic. 1.** Approximation index AMW254, st. units. from the time period of shock in injured rats at application Refortan and HAES-LX5% using a polynomial trend of second order.
Pic. 2. Approximation index AMW280, st. units. from the time period of shock in injured rats at application Refortan and HAES-LX5% using a polynomial trend of second order.

In rats, which do not receive treatment, the growth rate was observed AMW254 (with 0,033 ± 0,005 to 0,168 ± 0,03) and AMW280 (with 0,034 ± 0,004 to 0,18 ± 0,03) by 24 hours of shock period. Significant difference is noted AMW254 variation index (H = 22,9; p <0,0125) and AMW280 (H = 22,8; p <0,0125), depending on the timing of shock period. However, given the high rate of reliability approximation (R2 = 0,865) AMW254 and AMW280 index (R2 = 0,873), may predict its future growth. This confirms the fact that one of the significant indicators of endogenous intoxication determine the growth of average molecular weight (AMW250 and AMW280).

In rats, which got Refortan solution, observed growth rate AMW254 (with 0,028 ± 0,001 to 0,161 ± 0,001) and AMW280 (with 0,028 ± 0,001 to 0,161 ± 0,001) by 12 hour shock period. By 24 hours marked decrease in AMW254 to 0,1 ± 0,007 st. units. AMW280 and 0,101 ± 0,004 to mind. units. Significant difference is noted MSM254 variation index (H = 35,4; p <0,0125) and AMW280 (H = 32,6; p <0,0125), depending on the timing of shock period. However, given the moderately high reliability coefficient approximation (R2 = 0,767) AMW254 and AMW280 index (R2 = 0,770), may argue about the positive role reversal Refortan in shock after 12 hours.

In rats, which obtained solution HAES, observed growth rate AMW254 (with 0,034 ± 0,001 to 0,14 ± 0,008) and AMW280 (with 0,033 ± 0,0012 to 0,141 ± 0,001) by 12 hour shock period. By 24 hours marked decrease in MSM254 to 0,121 ± 0,0011 mind. units. and AMW280 to 0,121 ± 0,0012 mind. units. and given the high rate of reliability
approximation \((R^2 = 0.897)\) AMW\(_{254}\) and AMW\(_{280}\) index \((R^2 = 0.893)\), may predict its further decline. However, significant differences observed variation index AMW\(_{254}\) \((H = 35.5; p < 0.0125)\) and AMW\(_{280}\) \((H = 39.5; p < 0.0125)\), depending on the timing of shock period. It is therefore possible to state at more positive role HAES solution to reversal of shock after 24 hours of injury.

**Conclusions.**

1. When using a solution of HAES-LX5% growth rate variation average molecular weight in rats with combined injury of the abdominal cavity is most relevant depending on the time of traumatic shock period.

2. Dynamics of change of the average molecular weight of the contents in the study group, which carried out the replacement of blood loss solution HAES-LX5%, indicating its true cytoprotective effect of endogenous development and less toxicity compared with other groups in the study of experimental animals with simulated severe trauma of the abdominal cavity.

**Literature.**


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