Pandemic nature of the traumatism has been considered as an established fact [1] for a long time. Injury severity is increasing incessantly and, under such conditions, a problem of traumatic shock treatment is particularly pressing. Traumatic shock is fixed in 60-65% of trauma accident [2] and is a principal factor of early hospital lethality of injured patients [3]. In Ukraine, the application of infusion drugs based on sorbitol and sodium lactate has become one of the components of solution of the post-traumatic liquid resuscitation problem.

Described research is carried out for the purpose of the comprehensive application of the drug Reosorbilact® (Yuria-Pharm, Ukraine) by means of studying of its still unascertained effects and of comparison with the action of other drugs for liquid resuscitation.

**Purpose of the research:** improvement of treatment results in patients with traumatic shock by means of the scientific justification of the application of reosorbilact in the course of the clinical comparative research.

**Research objectives:** to compare the influence of infusions of reosorbilact, 0.9% NaCl and venofundin (BBraun, Germany) (hydroxyethyl starch solution with an average molecular weight of 130 kDa and degree of molecular substitution 0.42) on the parameters of hemostasis, fluid content of the chest and on the parameters of central hemodynamics in patients with traumatic shock.

**Materials and methods.** The research was carried out on the basis of Anesthesiology and intensive care department Municipal Clinical Hospital № 17 in Kyiv. 60 traumatized adult patients of both sexes with blood loss of III-IV grade, or with episode of decrease in systolic blood pressure < 90 mm Hg., after hospitalization they were randomized for the implementation of the planned clinical experiments. Randomization was not carried out for the traumatized with the heart injury, clinical indications of coagulopathy and the expected lethality rate during < 24 hours.

After the final cessation of the apparent bleeding or immediately after the establishment of central venous access in case of impossible implementation of a one-stage final hemostasis by surgery (for example, in case of the isolated skeletal trauma and the absence of apparent source of bleeding), infusion was started: in group I (n = 20) 800 ml reosorbilact with a rate of 50-55 ml / min., in group II (n = 20) – the identical infusion of 0.9% NaCl; in III (n = 20) group the infusion of 500 ml venofundin was carried out.

After the end of the studied drugs infusion which was lasting at the average for 13 min. (min 10; max 16), in all groups liquid resuscitation did not cease and continued with the influ-
sion of 0.9% NaCl at a rate of 18-22 ml / min. Among the groups the volume of poured 0.9% NaCl, from the moment of cessation of studied drugs infusion and to 60 min. of the research, it did not differ significantly and in total did not exceed 1200 ml. The studied group, basing on the absence of reliable statistical difference between the indices, were recognized as homogeneous by the age, sex, severity of injury, severity of condition when hospitalizing, type of injury, its structure, volume and composition of the previous infusion therapy.

Characterization of groups is partially shown in Table. 1.

Before the studied drugs infusion and immediately after its completion the following parameters of hemostasis were determined: activated partial thromboplastin time (APTT), prothrombin time (PT), international normalized ratio (INR) and number of platelets.

During 60 min. from the beginning of infusion by the impedance cardiography method (ICM) using DASH 3000 monitor (General Electrics, the USA) and SOLAR module the cardiac index, stroke index (SI), index-velocity (IV), heart rate (HR) fluid content of the chest (FCC) and the estimated oxygen delivery index (eDO₂I) were determined. For identification of gender-based changes FCC was investigated as in the main groups, as in the subgroups created, based on sex. Statistical processing was carried out in the software environment STATISTICA 6.0 (StatSoft Ink., 2001).

Depending on the type of data distribution the methods parametric (Student’s criteria, dispersion analysis ANOVA for repeated measurements with Newman-Keuls criteria) and non-parametric statistics (criterion Vilkoksona, Mann-Whitney U test, Kruskal-Wallis test) were used. In the text part of the article the data averaged by parametric distribution are presented as “the arithmetic mean (M) ± standard deviation (SD)”. When presenting the graphic information the standard error (SE) is provided. For some indices -95% and 95% confidence intervals (CI) are specified. Nonparametric averaged data are given as “median (lower quartile, upper quartile).” The average age for clarity is presented as “median (minimum-maximum).” All results of statistical processing are given with precision of the homologous experimental indices, which the arithmetic rounding rule was used for.

In the work the difference when the probability of a false null hypothesis refutation is less than 5 % (p < 0.05) was considered statistically significant.

<table>
<thead>
<tr>
<th>Group</th>
<th>Average age (years)</th>
<th>Gender</th>
<th>ISS (points)</th>
<th>APACHE II (points)</th>
<th>Character of trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-st (Reosorbiact)</td>
<td>29.5 (19-57)</td>
<td>Male – (14; 70%)</td>
<td>29±100</td>
<td>15</td>
<td>Blunt – 15 (75%)</td>
</tr>
<tr>
<td>800 ml</td>
<td></td>
<td>Male – (6; 30%)</td>
<td>(9-57)</td>
<td>(11;17)</td>
<td>Penetrating 5 (25%)</td>
</tr>
<tr>
<td>II-nd (0.9% NaCl)</td>
<td>24.5 (15-52)</td>
<td>Female – (14; 70%)</td>
<td>27±10</td>
<td>15</td>
<td>Blunt – 15 (75%)</td>
</tr>
<tr>
<td>800 ml</td>
<td></td>
<td>Female – (6; 30%)</td>
<td>(10-50)</td>
<td>(11;19)</td>
<td>Penetrating 5 (25%)</td>
</tr>
<tr>
<td>III-rd (Venofundin)</td>
<td>28.5 (19-47)</td>
<td>Male – (14; 70%)</td>
<td>28±7</td>
<td>14</td>
<td>Blunt – 15 (75%)</td>
</tr>
<tr>
<td>500 ml</td>
<td></td>
<td>Female – (6; 30%)</td>
<td>(16-41)</td>
<td>(10;17)</td>
<td>Penetrating 5 (25%)</td>
</tr>
</tbody>
</table>

**Fluid content of the chest**

**Results and Discussion.** The range of normal values FCC parameter depends on gender. For men it is 30-50 kOm⁻¹, for women – 21-37 kOm⁻¹ [4]. Averaged value of the initial FCC in men (n = 42) of all groups (Fig. 1) was in the normal range (46±5 kOm⁻¹). Averaged value of the initial FCC in women (n = 18) (Fig. 2) was 39 kOm⁻¹ (29;43) and unauthentically (p = 0.088) exceeded the upper limit of the norm. Despite the unreliability of excess, we believe that we should pay attention to the fact that high FCC in women in a state of traumatic shock, because it may indicate the presence of a gender-based response of the female body on the trauma and prehospital resuscitation as an increase of hydration of the chest organs (pulmonary parenchyma in the first place) over the norm.

Dynamics FCC after studied drugs infusion is shown in Fig. 3. In all studied groups FCC significantly increased (p<0.05) and remained significantly higher than the norm during 60 min. Maxima were observed at the 25-th minute in groups of reosorbiact and venofundin...
Glumcher F.S., Chernyshov V.I. Application of Reosorbilact in the therapy of traumatic shock

(4% and 3% from the corresponding initial value) and at the 15-th minute in group 0.9% NaCl (+4%). According to all the measurements the significant difference between the studied drugs was absent (p>0.05).

It should be noted that this fact, and also the absence of any fact of FCC reduce in the group of reosorbilact, denies a working hypothesis about the ability of reosorbilact to reduce the hydration of the chest organs (especially lung parenchyma), which was previously proposed by the authors on the basis of a pilot research results [5]. The difference between the pilot and described researches, in our opinion, can be explained by the design optimization of the last one and by the increase in the number of observations. Concerning the reasons of the FCC increase in all groups, even though we can not completely exclude that the obtained moderate increase (max+4%) could occur at the expense of the FCC intravascular component augmentation, increase of hydration of the chest organs extravascular sector as a more probable cause because in the first case the FCC increase would not be so prolonged (during 60 min.) and would be accompanied by a noticeable fluctuations (for example, immediately after cessation of infusion). A final answer to this question can be obtained in the case of a similar research implementation using the transpulmonary thermodilution technique [7].

**Indicators of central hemodynamics**

In the research for the preload level assessment a directly measurable ICG indicator of the index-index-velocity (IV) was used. The IV is the most important value of bloodstream velocity in the aorta at a certain time. The range of normal values – 35-65 sec⁻³. The IV dynamics is presented in Fig. 4. Average initial values in all the groups, as it was expected, were below the norm (median (quartile range)): in the group I – 33 sec⁻³ (25; 41); in the group II – 32 sec⁻³ (29; 36); in the group III – 33 sec⁻³ (30; 36). After the beginning of infusion the significant IV increase was observed in all the groups, but the maximum preload increase in reosorbilact groups (+ 37% at 15 min.) and in venofundin groups (+ 35% at the 25-th min.) it significantly (p<0.05) exceeded the maximum in 0.9% NaCl group (+ 19% at the 10-th min.). The effect of the preload increase in reosorbilact and venofundin groups was significantly more prolonged (p<0.05) than after infusion of 0.9% NaCl, whereof the significant difference from the initial value to 60 minutes inclusive of the observation indicates (p < 0.02 in the group I, p<0.001 in the group III). In the group of 0.9% NaCl reliability of such difference was observed only before 30 minutes inclusive (p<0.02). According to all the measurements the difference between the groups of reosorbilact and venofundin was proved to be unreliable (p>0.05),
Fig. 3. Fluid content of the chest

Fig. 4. Index-velocity
but the preload decrease velocity in reosorbilact group was higher, despite the greater volume of infusion.

The range of normal values of cardiac index accepted in the research was 2.5-4.5 l/min/m² [4]. Average ascending values of the cardiac index answered the lower limit of the norm (group III – 2.5±0.4 l/min/m², CI 2.4-2.7), or were smaller than the norm (I and II group – 2.4±0.4 l/min/m², CI 2.2-2.6). Similar cardiac index values are typical for patients who are in a shock condition. After the beginning of studied drug infusion the cardiac index increase was observed in all the groups (Fig. 5). In groups of reosorbilact and venofundin significant cardiac index augmentation was observed already at 5 min. (p<0.001). Maximum increase in the cardiac index in reosorbilact group was observed at 25 min. and was 30% of the initial value (p<0.001). In the group of venofundin maximal increase was recorded at a level of 18% (p<0.001) for 45 min. of the experiment. Regardless of visually significant differences, the significant difference between reosorbilact and venofundin before 45 min. inclusive was not obtained in any observation, although the difference was close to the threshold of reliability at 15 min. (p=0.087). Since 45 min. the cardiac index in the group of venofundin exceeded the cardiac index in the group of reosorbilact, and at 60 min. significantly more important value of the cardiac index in the group of venofundin (p = 0.042). Significant cardiac index increase in the group of 0.9% NaCl was observed only once in 10 minutes. (+8%, p=0.001). According to all the measurements (except the initial) the cardiac index in the group of 0.9% NaCl was significantly inferior as to reosorbilact (p<0.05) as to venofundin (p<0.05, except 10 min. with p=0.147).

In all study groups at a point of the research beginning patients with tachycardia were dominating (Fig. 6). Ascending HR values were: in the group I 105±16 beats/min. (CI 98-113); in the group II 100±16 beats/min. (CI 93-108); in the third group 103±13 beats/min. (CI 97-109). After reosorbilact infusion already at 10 min. the significant increase in heart rate (p=0.02) was observed, which lasted throughout the observation period, and inn a maximum of 20 min. was 117±16 beats/min. (+11%; CI 109-124; p<0.001).
HR in the group of reosorbilact from 10 and to 60 min. inclusive, was significantly greater than in the other groups (p<0.05). In contrast to reosorbilact, in venofundin group after the drug infusion before 60 min. inclusive was observed a significant HR moderation with a minimum at 10 min. 94 ± 8 beats / min. (-9% CI 90-98, p<0.001). In the group of 0.9% NaCl a slow HR increase was observed. Significant increase by 5% was recorded at 60 min. (p=0.001). Statistically significant difference between groups of 0.9% NaCl and venofundin by HR was not obtained in any measurement.

The initial average value of the stroke index (SI) in all the groups (Fig. 7) were significantly lower than the norm accepted in the research (35-65 ml / m2): in the group I 23±4 ml/m2 (CI 21-25); in the group II 24±5 ml/m2 (CI 22-27); in the group III 25±4 ml/m2 (CI 23-27). From the beginning of infusion of all the studies drugs the SI significantly increased. The greatest (31±4 ml/m2, CI 29-32, 23% at 60 min.) and the most significant increase was observed in the group of venofundin (p<0.001).

Significant increase in the SI in the group of reosorbilact was observed at 5 min. and lasted for 30 minutes. including a maximum at 5 min. 27 ± 4 ml/m2 (+18% CI 25-29, p<0.001).

Beginning with the 45th minute, the SI in this group did not differ significantly from the initial values. In the group of 0.9% NaCl the SI has changed significantly towards the increase once for 10 min. of the observation by 8% (p=0.016) and henceforward has tended to decrease. The other measurements in this group has not differed significantly from the ascending values.

Intergroup comparison has revealed the reliability of the difference between venofundin and reosorbilact at 10.25 - 60 min. (p<0.05), between venofundin and 0.9% NaCl according to all the observations between reosorbilact and 0.9% NaCl – at 30 min. (p=0.047).
The estimated oxygen delivery index (eDO$_2$I) – ICG parameter, calculated by the formula (1) and by the norm is 500-600 ml/min/m$^2$ [7].

$$eDO_2I = CT \times \text{SpO}_2 \times 1.38 \times Hb$$

where $\text{SpO}_2$ – saturation of capillary blood;
Hb – hemoglobin of capillary blood in g/l;
CT – cardiac index in l/min/m$^2$.

In all the groups the initial average values of eDO$_2$I were lower than the norm: in the group I – 321±88 ml/min/m$^2$ (CI 280-362); in the group II – 31±66 ml/min/m$^2$ (CI 287-349); in the group III – 344±67 ml/min/m$^2$ (CI 312-376). During the whole period of observation a normalization of this index was not achieved in any group.

The eDO$_2$I dynamics (Fig. 8) after the beginning of the studied drugs infusion was substantially stipulated by the changes in CT as a component of the formula (1) which changes the most significantly as a result of the infusion loading. The significant increase of the eDO$_2$I is recorded in all the groups. In the group of reosorbilact maximal increase was observed at 25 min. – 416±102 ml/min/m$^2$ (+30%; CI 287-349; $p<0.001$). In the group of venofundin maximal increase of eDO$_2$I was observed at 45 min. – 404±76 ml/min/m$^2$ (+17%; CI 368-439, $p<0.001$). In both of groups, all the measurements were significantly ($p<0.05$) greater than the initial ones. The significant difference between reosorbilact and venofundin was not obtained in any of the measurements. Maximal significant increase of eDO2I in the group of 0.9 % NaCl recorded at 10 min. (347±75; +9%; CI 312-382; $p<0.001$). Starting from 20 min. inclusive in this group the eDO$_2$I values did not significantly differ from the initial ones.

Analyzing the obtained hemodynamic parameters, especially it should be noted that the infusion carried out in the groups of reosorbilact and venofundin, allowed to eliminate hemodynamic instability (judging from the values of the cardiac index), but did not lead to the final stabilization and compensation of the blood loss, so far as the normalization of SI and eDO$_2$I
was not achieved. Hemodynamic effect of the studied volume of 0.9% NaCl should be generally recognized as apparently insufficient to the resuscitation of patients with traumatic shock, as in this group was reached only the least allowable hemodynamics compensation.

The action of reosorbilact, in comparison with venofundin should be recognized as more quick and “aggressive” but less prolonged in time that is most probably associated with the duration of the drug’s being in the bloodstream.

The cardial index increase in the group of reosorbilact was principally due to the HR increase. The similar effect can be probably explained by the solution’s hyperosmolarity (900 mOsm/l), by the rapid preload increase and, perhaps, similarly to the 7.5% NaCl [8], by the ability to stimulate the rapid release of catecholamines.

The significant HR increase as a result of the rapid infusion of reosorbilact requires caution regarding its application in traumatized patients with high ascending level of heart rate.

**Coagulation system**

Average values of coagulation indicators are presented in Table 2.

At the beginning of the research the average activated partial thromboplastin time (APTT) in all the groups was within normal limits (35-45 sec). The number of platelets was also compatible with the normal value. Prothrombin time (PT) and international normalized ratio (INR) in all the groups at the beginning exceeded the accepted normal values (14-18 sec and 0.9-1.1 respectively). Since it is known that an isolated (APTT without increase) PT increase is characteristic for the hemodylution [9], most likely the cause of this phenomenon was the previous infusion therapy on the pre-hospital stage.

Reosorbilact infusion was not accompanied by significant changes of any of the parameters (Figure 9-11), which may be an indication of the absence of effects on coagulation hemostasis in case of trauma in the studied volume of this drug.
In the group of 0.9% NaCl significant changes of all the indicators of coagulation hemostasis sideward the hypercoagulation (Fig. 9-11) were recorded. Such dynamics can be considered as procoagulant effects of 0.9% NaCl infusion, although the absolute values of coagulation indicators after the infusion did not correspond to hypercoagulative condition.

Pronounced significant increase in APTT (+18%), PT (+16%) and value of INR (+16%) was observed after venofundin infusion (Fig. 9-11). The values of all the parameters of coagulative hemostasis were greater than the norm and in some cases the PT and INR values increased more than 1.5 times above the norm, that is considered theoretically as a coagulopathy threshold [10].
All the studied infusion drugs have demonstrated the absence of effects on the platelets number (Fig. 12). This may give evidence of the application safety of the studied volumes of reosorbilact, 0.9% NaCl and venofundin for traumatic shock accompanied by thrombocytopenia.

Conclusions: 1. Reosorbilact infusion in the amount of 800 ml in traumatic shock is not accompanied by effects on the coagulation hemostasis system, whereas the infusion of 0.9% NaCl equal volume is followed by a tendency to hypercoagulation and venofundin infusion in the volume of 500 ml – the hypo-coagulation as a result of the hemodilution. 2. Infusion of Reosorbilact and of 0.9% NaCl for traumatic shock leads to the significant FCC increase without significant difference according to the influence of the studied drugs. 3. Reosorbilact has pronounced hemodynamic effects and increases the oxygen delivery, which makes justified its application in traumatic shock, but by the duration of its effect it is inferior to venofundin. 4. With more pronounced tachycardia the slower administration of reosorbilact is more reasonable.

Literature


