INTRODUCTION

Polytrauma or multiple organ damage is associated with shock and organ failure, which is injuring patients severely and can lead quickly to death if untreated [1,2]. It is well known that every tissue damage is related to systemic inflammation, oxidative stress, and endothelial dysfunction. A severe mechanical injury causes an increased proinflammatory mediators and cytokines levels. Among them, the overproduction of nitric oxide and its oxidation products play a key role in tissue damage.

The aim: To evaluate the changes in dynamics of some ornithine cycle components levels during acute period of polytrauma.

MATERIALS AND METHODS

We measured standard biomechanical parameters and serum levels of NO, sum of nitrite and nitrate (NOx), L-arginine, arginase, and peroxynitrite. According to the ISS, the study included patients with moderate (n=15) to severe (n=15) polytrauma.

RESULTS

In 24 hours after polytrauma on the background of intensive care, it was observed significant increasing of NO, NOx, and arginase levels (severe cases) with decreasing of L-arginine and peroxynitrite levels.

CONCLUSIONS

Elevated NO and NOx serum levels in patients with polytrauma is associated with increasing of arginase activity with decreasing of L-arginine and peroxynitrite levels on the background of intensive care.

KEY WORDS: polytrauma, nitric oxide, arginine, arginase, peroxynitrite
ratory and instrumental studies were conducted to assess the clinical signs and severity of traumatic shock at the time of ICU admission.

Diagnostic studies and consecutive therapy were carried out in accordance with the International Trauma Life Support guidelines (ATLS®).

The provided anti-shock therapy included hemostatic measures, adequate anesthesia and securing of an adequate gas exchange. The central venous access was provided by means of catheterization of the subclavian vein. Furthermore, a nasogastric tube and a urinary catheter were placed. The volume and rate of infusion therapy was determined by the deficit of circulating blood volume. Post-traumatic hemorrhagic anemia was restored with by means of blood transfusion. Emergency surgical interventions were carried out in acute life-threatening conditions. All patients routinely received a correction of water-electrolyte balance and metabolic disorders, respiratory therapy as indicated, antibacterial therapy, analgesia, correction of hemostatic disorders and symptomatic therapy as required.

The biochemical analysis of blood was carried out by the laboratory of the Department of Biochemistry of the Lviv National Medical University (LNMU). The analysis of NO, NOx, L-arginine, arginase, and peroxynitrite in serum was carried out on admission and after 24 hours of intensive care.

The blood serum was analyzed for the concentration of nitrite anions (NO2-) (μmol/l), the final stable product of the NO metabolism and the sum of nitrite NO + NO3 (NOx) (μmol/l), using cooled centrifuged blood and Griess reagent [15].

The investigation of arginase activity (μmol/min×ml) was performed according to the method of Geyer J.W., 1971 [16]. Enzyme activity was determined by the amount of urea formed in the reaction. Investigation of the content of L-arginine (μg/ml) in blood plasma was carried out by the method of Aleinikova TL, Rubtsova GV 1988 [17].

Determination of serum peroxynitrite (ONOO) ONOO-mediated nitration of phenol was measured as described by van Uffelen et al. [18].

The levels of urea (mmol/l) and total protein (g/l) in the blood plasma were determined by a BioChem FC-360 auto-biochemical analyzer using a completely enzymatic method of kinetic determination of urea (GLDH Method) and a photocolorimetric determination of the total protein (Biuret Method).

Continuous characteristics were represented using means and standard deviations. Independent Student t-test was used to compare discrepancies between the different groups. Analysis of data was performed and expressed as mean ± SD.

**RESULTS AND DISCUSSION**

During analyses of damage severity it was revealed that among investigated group of patients major were modest damage (ISS and APACHE II). Intensive care therapy and surgical treatment in patients during first 24 hours leads to improvement of hemodynamic parameters. On the second day was noticed increase of systolic blood pressure and decrease of heartburn. During first 24 hours, diuresis increased from 800 to 1300 ml. Standartization of hemodynamic parameters and 24-hours diuresis evidenced about patients improvement from traumatic shock.

**Table I.** Comparable levels of biochemical parameters in patients with moderate polytrauma in different trauma periods

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Acute period</th>
<th>After 24-hours</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/L</td>
<td>100,5±2,4, p&lt;0,05</td>
<td>112,4±1,9, p&lt;0,001</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Hematocrite, %</td>
<td>28,8±1,3</td>
<td>30,2±0,9</td>
<td>p&gt;0,5</td>
</tr>
<tr>
<td>White blood cells, x10^9/L</td>
<td>8,8±0,4</td>
<td>11,0±0,4</td>
<td>p&lt;0,01</td>
</tr>
<tr>
<td>Urea, mmol/L</td>
<td>8,4±1,1</td>
<td>8,8±0,6, p&lt;0,05</td>
<td>p&gt;0,5</td>
</tr>
<tr>
<td>Protein, g/L</td>
<td>58,5±1,2</td>
<td>56,3±1,3, p&lt;0,05</td>
<td>p&gt;0,5</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5,5±0,1</td>
<td>7,2±0,4</td>
<td>p&lt;0,01</td>
</tr>
<tr>
<td>Total Bilirubin, mmol/L</td>
<td>12,2±0,9</td>
<td>12,5±0,8</td>
<td>p&gt;0,5</td>
</tr>
</tbody>
</table>

**Table II.** Comparable levels of biochemical parameters in patients with severe polytrauma in different trauma periods

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Acute period</th>
<th>After 24-hours</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/L</td>
<td>91,2±2,8</td>
<td>84,9±2,9</td>
<td>p&gt;0,05</td>
</tr>
<tr>
<td>Hematocrite, %</td>
<td>31,8±1,4</td>
<td>28,7±0,8</td>
<td>p&gt;0,05</td>
</tr>
<tr>
<td>White blood cells, x10^9/L</td>
<td>9,9±0,6</td>
<td>12,6±0,6</td>
<td>p&lt;0,05</td>
</tr>
<tr>
<td>Urea, mmol/L</td>
<td>8,4±0,7</td>
<td>12,2±0,8</td>
<td>p&lt;0,05</td>
</tr>
<tr>
<td>Protein, g/L</td>
<td>56,9±1,3</td>
<td>50,5±1,7</td>
<td>p&lt;0,05</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>6,2±0,3</td>
<td>7,7±0,3</td>
<td>p&lt;0,01</td>
</tr>
<tr>
<td>Total Bilirubin, mmol/L</td>
<td>14,4±1,2</td>
<td>15,8±1,0</td>
<td>p&gt;0,5</td>
</tr>
</tbody>
</table>
Fig. 1. Comparable levels of NO, NOx in patients with moderate and severe polytrauma in acute periods.

Fig. 2. Comparable levels of L-arginine in patients with moderate and severe polytrauma in acute periods.

Fig. 3. Comparable levels of arginase in patients with moderate and severe polytrauma in acute periods.
(leucocitosis, neutrofilosis), hyperglycemia, hyperfibrinemia, and subfebrile body temperature. Blood biochemical parameters during hospitalization were in the range of normal levels. But albumin and prothrombin index (PTI) decrease on the second day while fibrinogen and glucosae increase (Table I).

In both groups of patients with moderate and severe polytrauma, there was observed increasing of NO and NOx levels after 24 h of intensive care. In patients with moderate polytrauma, level of NO increased from 0.328±0.023 µmol/L to 0.425±0.033 µmol/L (p < 0.01) and level of NOx increased from 2.173±0.168 µmol/L to 2.652±0.181 µmol/L (p < 0.01). In patients with severe polytrauma, level of NO increased from 0.365±0.021 µmol/L to 0.455±0.025 µmol/L (p < 0.01) and level of NOx increased from 2.40±0.15 µmol/L to 3.00±0.14 µmol/L (p < 0.01) (Figure 1).

In both groups of patients with moderate and severe polytrauma, there was observed decreasing of L-arginine levels after 24 h of intensive care. In patients with moderate polytrauma, level of L-arginine decreased from 64.14±1.44 µg/mL to 59.05±1.08 µg/mL (p < 0.01). In patients with severe polytrauma, level of L-arginine decreased from 70.23±1.42 µg/mL to 59.28±1.24 µg/mL (p < 0.01) (Figure 2).

In group of patients with moderate polytrauma, there was not observed statistically significant difference in arginase levels after 24 h of intensive care. However, arginase levels significantly increased from 0.271±0.08 µmol/min×mL to 0.288±0.007 µmol/min×mL in patients with severe polytrauma (p < 0.01) (Figure 3).

In both groups of patients with moderate and severe polytrauma, there was observed decreasing of peroxynitrite levels after 24 h of intensive care. In patients with moderate polytrauma, level of peroxynitrite decreased from 20.42±0.34 µmol/L to 16.96±0.36 µmol/L (p < 0.01). In patients with severe polytrauma, level of peroxynitrite decreased from 22.88±0.64 µmol/L to 17.97±0.40 µmol/L (p < 0.01) (Figure 4).

When comparing some indicators of the ornithine cycle at moderate and severe polytrauma, there was observed a general tendency of changes in these indicators, as well as features of changes in the course of severe polytrauma were shown.

For acute period of polytrauma, there is observed significant increasing of NO and its oxidation products levels after 24 hours that can be associated with increased expression of inducible isoforms of NO-synthase (Beitl et al., 2016).

However, there was observed a significant decreasing of L-arginine and peroxynitrite levels with a substantially increasing of arginase in patients with severe polytrauma.

It should be noted that these metabolic processes are more pronounced in severe polytrauma that is demonstrated by significant changes in L-arginine, arginase, and peroxynitrite levels compared to these parameters at moderate polytrauma. These results are confirmed by negative correlation between arginase and NOx (r = -0.52) (Caldwell 2018).

Therefore, the presented data demonstrate that in acute period of polytrauma with systemic inflammation processes there is simultaneously occurring functions recovery via arginase regulatory activity regarding L-arginine level with further decreased NO synthesis.

CONCLUSION
Elevated NO and NOx serum levels in patients with polytrauma is associated with increasing of arginase activity with decreasing of L-arginine and peroxynitrite levels on the background of intensive care.

REFERENCES

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Conflict of interest:
The Author declare no conflict of interest.

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