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**Mykolenko A.Z.***SHEE "I. Horbachevsky Ternopil State Medical University of Ministry of Health of Ukraine", Department of Pathologic Anatomy, Autopsy Course and Forensic Pathology, Ternopil, Ukraine, amykolenko@gmail.com***CHANGES OF CONCENTRATION OF MIDDLE MASS MOLECULES IN BLOOD SERUM IN THE EARLY DAYS OF ISOLATED ORTHOPEDIC TRAUMA COMPLICATED BY BLOOD LOSS**

**Abstract.** *Isolated orthopedic trauma (fracture of thigh bone) at the early period of traumatic disease is accompanied by an increase in the content of the middle mass molecules in blood with a maximum level on the 3-d day and normalization in 7 days. Under these conditions, additional blood loss enhances the level of endogenous intoxication, and is accompanied by a significant accumulation of fractions of middle mass molecules in the blood, and in 7 days their content does not reach the control level.*

**Key words:** *isolated orthopedic trauma, blood loss, endotoxycosis.*

**Introduction.** There is a considerable increase in the level of traumatism complicated by blood loss for last years. In the pathogenesis of critical states, accompanied by metabolic disorder and natural detoxification, endotoxemia, caused by traumatic shock, hypovolemia, systemic hypoxia and lipid peroxidation, plays a significant role [1]. Middle-molecular products of proteolysis, which in modern literature are called middle mass molecules (MMM), are the general biochemical marker of physiologically active components. Evaluation of content of these molecules in blood and other biological fluids is the sensitive indicator of syndrome of multiple organ failure and systemic organism response to inflammation [2,3]. These molecules are peptides, glycopeptides, degradation products of fibrinogen, albumin, thrombin, collagen fragments, other protein substances and derivatives of lipids, phospholipids, etc. Manifestations of biological activity of middle-molecular peptides are quite numerous. They have vaso-, cardio, neuro- and immunosuppressive properties, inhibit such metabolic processes as mitochondria respiratory, DNA synthesis in hepatocytes, synthesis and utilization of glucose, hemoglobin synthesis, activity of some enzymes. Action of MMM disturb transport of amino acids, lipid peroxidation in the brain [4,5]. MMM

accumulation supposed to be the result of insufficient activity of exopeptidases, which normally are responsible for degradation of peptides in blood [14].

**Objective:** to study the features of changes of concentration of MMM at the acute phase and at the early days of traumatic disease on a background of isolated orthopedic trauma, and their dependence on the intensity of blood loss.

**Materials and methods.** The study was performed on 80 nonlinear white male rats, which were fed a standard diet in a vivarium. The animals were divided into 4 groups of 8 each. The first group consisted of rats with simulated isolated orthopedic trauma, which was the closed fracture of thigh bone by dosed kick with specially designed device. The second group consisted of the rats with the blood loss of 20-22% of the circulating blood volume by intersection of the femoral vein. The rats with both these damages were in the third group. And the intact rats were in the forth control group. All traumas were made under the thiopental sodium anesthesia (40 mg·kg<sup>-1</sup> of body weight). The animals were taken out of the experiment in 1, 3 and 7 days after the start of post-traumatic period by a total bloodletting from heart under the same anesthesia. Content of MMM fractions in blood serum were determined at the wavelengths 254 and 280 nm (MMM<sub>254</sub>, MMM<sub>280</sub>) [4]. Statistical significance

of differences between experimental and control groups was evaluated using the program STATISTICA 10.0 ("StatSoft, Inc.", USA).

**Results and discussion.** Studies showed (Figure), that under the effect of trauma the content of the studied MMM fractions in the blood serum increases considerably and reaches the maximum level on the 3<sup>d</sup> day: MMM<sub>254</sub> is higher on 84.1% than in control group, MMM<sub>280</sub> - on 107.2% (p<0.05). In 7 days the indexes decrease and become smaller than the control level (on 19.6%, p<0.05 and on 12.4%, p<0.05 respectively).

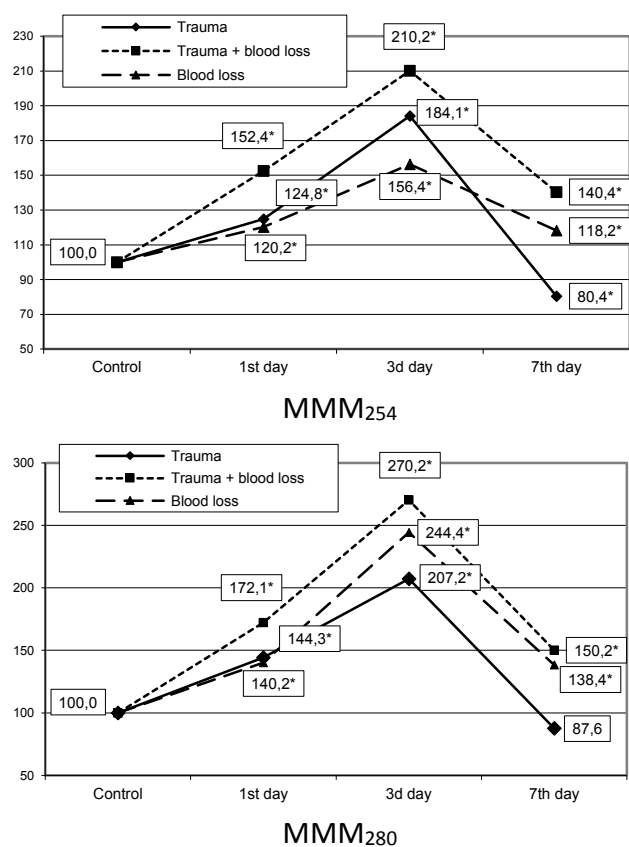


Figure – Changes of content of MMM<sub>254</sub> i MMM<sub>280</sub> in the blood serum (percent of the control level) on a background of the isolated orthopedic trauma, blood loss and them together at the acute phase and at early days of traumatic disease (\* - differences compared to the control group are statistically significant, p<0.05).

At the blood loss the indexes increase considerably too compared to the control group, reaching the maximum level on the 3<sup>d</sup> day. In one day their values were nearly equal to the ones of the animals with isolated orthopedic trauma (p>0.05). In 3 days the content of the MMM<sub>254</sub> is much smaller, and the content of the

MMM<sub>280</sub> is much higher than the ones of animals with isolated orthopedic trauma (p<0.05). In 7 days the contents of both fractions are much higher than the ones of animals with isolated orthopedic trauma (p<0.05).

Under the combination of isolated orthopedic trauma with blood loss the studied indexes are statistically significantly higher than the ones of control group and groups with separate traumas (p<0.05) during all the observation time. Dynamics of their change is the same: maximum level is on the 3<sup>d</sup> day (in 2.1 and 2.7 times respectively, p<0.05) with the following decrease, which does not reach the control level. Under these conditions in 7 days the content of MMM<sub>280</sub> is on the same level of the animals with blood loss (p>0.05).

Obtained results show, that all the traumas are accompanied by metabolic disorder, which leads to the accumulation of the products of protein proteolysis – MMM, that indicates the consistency of the revealed disorder. The dynamics of their changes under the each studied trauma are the same: manifestation in 3 days and following decrease in 7 days, which indicates the intensification of the processes of detoxification. Under these conditions on a background of the isolated orthopedic trauma the content of the MMM fractions becomes lower than control, which is the sign of the excessive adaptation and compensatory response of the traumatized organism, aimed at the restore of homeostasis. The phenomenon of such excess is obviously a general biological phenomenon in case of damage or irritant of moderate intensity. Attention should be paid to the fact, that the amplitude of the disorders of the content of the MMM<sub>280</sub> fraction is higher. According to literature data, this fraction contains substances with aromatic groups, which detoxification occurs in the liver and lungs, where they are biologically transformed by monooxygenase system or change in conjugation reactions with following removal through the kidneys, skin, gastrointestinal tract [5]. Blood loss intensifies the accumulation of the MMM in blood and even compared to the isolated orthopedic trauma in 3 days the content of the MMM<sub>280</sub> fraction is higher, and in 7 days

the same occurs to the both fractions. So, the leading role in the genesis of their appearance is played by the development of systemic hypoxia, which is not compensated to the 7<sup>th</sup> day of the post-traumatic period. Under the conditions of the combination of both traumas the amplitude of the disorders is higher, that points to the effect of summation of both traumatic injuries, where getting of molecules damaged cells into the bloodstream, hypercatecholaminemia, stimulation of metabolism, accumulation of inflammatory cytokines with impaired blood flow in the microvasculature play the leading role, which in its turn deepens systemic hypoxia [5,6]. Additional "vicious circle" closes and deepens the pathological process.

**Conclusions.** Additional blood loss deepens the level of the endogenous intoxication at the isolated orthopedic trauma, which is accompanied by the considerable increase in the content of the MMM254 and MMM280 fractions with the maximum level on the 3d day and the decrease in 7 days, which does not reach the control level.

**Prospects for further research.** The deepening of the pathological process at the combination of isolated orthopedic trauma with blood loss require for searching for adequate methods of systematic correction at the acute period of traumatic disease.

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