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Biochemical Aspects of Preclinical Prediction of the Severity of the Knee Joint Injuries in Acute Period

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Abstract- **Early detection of markers of joint damage in order to predict the course of the inflammatory process and the risk of developing post-traumatic osteoarthritis is one of the urgent problems of traumatology and orthopedics. Determining the molecules of average mass and necrotic substances in the hemosynovial fluid of the injured knee joint demonstrates a significant association with the severity of the injury, the severity of the inflammatory process and the progression of post-traumatic osteoarthritis. Increasing the level of necrotic substances in hemosynovial fluid to 1.6-2.0 U/ml, 45.4% corresponds to significant damage to the intra-articular structures and leads to the development of the inflammatory process; an increase in excess of 2.0 U/ml is an indicator of severe joint injury and leads to a complicated postoperative course. The defined markers are the products of deep cell destruction, the level of necrotic substances increases during inflammatory and destructive processes and is used as a marker of endotoxicosis processes with high prognostic efficacy (specificity: 89.5%).**

Keywords: osteoarthritis; endotoxicosis; anterior cruciate ligament rupture; hemosynovial fluid; knee-joint injuries; hemarthrosis.

I. Introduction

In most cases, acute injury of the knee joint is accompanied by the appearance of hemarthrosis, the causes of that damage to the meniscus, dislocation of the patella, damage to the cartilage and subchondral fractures [1, 2]. Trauma is a proven risk factor for osteoarthritis (OA), which leads to disability [3, 4]. According to the literature, after a meniscus rupture requiring surgical intervention, OA develops in 50% of cases in patients [5].

Studies of the molecular mechanisms of the development of post-traumatic OA have shown the leading role of the activation of pro-inflammatory cytokines (IL-1 and TNF-α) in the focus of damage [6]. The effect of intra-articular fractures on inflammation of the synovial membrane remains unknown, although synovial pathology is crucial in the development of various forms of OA [1, 9].

Assessment of post-traumatic hemarthrosis of the knee joint only by clinical methods cannot demonstrate the seriousness of the injury. In such cases, arthroscopy is invaluable for the determination of concomitant damage and is significantly superior in magnitude to magnetic resonance imaging (MRI). The advantage of arthroscopy is at the same time carrying out not only diagnostic, but also medical procedures [7].

It should be noted that currently there are no prognostic biochemical markers that can reliably predict the course of the inflammatory process and the severity of injuries. In this regard, the identification of early markers of joint damage, prediction of the inflammatory process and the risk of OA is one of the urgent problems of traumatology. Identification of biomarkers potentiating the development of the inflammatory process and OA has so far focused mainly on matrix degradation products and, as a rule, in individuals with established OA. Although some biomarkers show statistically significant associations with the severity of injury and the progression of post-traumatic OA [8], however, no clear criteria for preclinical prediction have yet been developed. So, according to the growth of the content of individual cytokines (IL1, IL6, TNF-α), the activity of the inflammatory process in the joints is judged [9]; however, it is practically impossible to speak about their effector functions [10]. The known method determines the nature of the course of post-traumatic hemarthrosis according to the biochemical parameters of the synovial fluid: seromucoid level, markers of lipid oxidation, antioxidant activity and inflammation [11, 12], but their prognostic significance has not been established.

The purpose of the research is to evaluate the diagnostic and prognostic significance of the content of oligopeptides (E-254) and necrotic substances in hemosynovial fluid, for preclinical assessment of the severity of injury to the knee joint in the acute period before arthroscopy.

II. Materials and Methods

To accomplish this goal, we were researching on 20 patients with posttraumatic hemarthrosis who received treatment in the Department of Traumatology of the 2nd TMA clinic. Patients were predominantly male (16 men and 4 women). The average age of patients was 36.6±2.9 years (from 18 years to 47 years); the

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largest number of patients falls on the age group of 24-36 years, patients of young working age. In 80% of cases, the injury had a household character. All patients were examined shortly after the injury of the knee joint, the average time from the moment of injury to the examination was 3 days. Inclusion criteria were clinically significant acute knee injury in the last 3 weeks; effusion of the knee joint, confirmed clinically and with MRI; the presence of ≥1 specified structural injury on MRI (Siemens, 1.5 Tesla). Exclusion criteria were the presence of pronounced OA of the knee joint (III-IV degree according to Kellgren-Lawrence, 1978); inflammatory/septic arthritis of the affected knee; active or treated systemic inflammatory disease; recent infection; pregnancy.

All patients had baseline clinical signs of hemosynovitis and MRI findings. A number of structural injuries of the knee in a group of patients were classified after arthroscopic surgery with an addition to the conclusion of an MRI. The most common types of injury were a meniscus rupture, anterior cruciate ligament rupture (ACLR), or simultaneous injury. Of the total number of patients in 100% surgical treatment was carried out, 95% of them <24 hours after admission to hospital treatment.

All types of injuries were identified and listed an increasing order of injury, diagnosed using arthroscopy (Karl Storz arthroscopic stand) and MRI. Severe injury was defined as a combined torn ligament (>1), meniscus damage, fracture or dislocation. Clinically, the volume of effusion was assessed as small (up to 50 ml), medium (up to 250 ml) or large (over 250 ml).

When arthroscopy was carried out to patients, in addition to the diagnostic purpose, and therapeutic manipulations, the state of the synovial membrane and the cartilage cover of the knee joint was assessed. Assessment of knee joint case was carried out according to the following criteria:

- The state of the menisci.
- Gap nature was evaluated according to the classification of the ISAKOS Classification of meniscal tears (2011).
- With the definition of the location.
- Nature and features of the gap.
- Cartilage layer condition of the knee joint was assessed by Bauer and Jackson (1988) as the classification, most suitable for the assessment of acute injury.
- The state of Hoff's body.
- The presence of a bruise, hematoma, local structure disorder.
- In case of acute injury, the synovial membrane has signs of damage in the form of a hematoma;
- The presence of bleeding vessels, swelling of synovial villi.
- The presence of hemosynovial fluid, volume and character.

Upon admission to inpatient treatment, a puncture of the knee joint was performed, and the accumulated synovial fluid was collected with a sterile syringe. In the synovial fluid, the average molecular weight (AMW) content after precipitation of proteins with trichloroacetic acid (TCA) was determined by spectrophotometric ways on 254 nm wavelength. The result was expressed in units of optical density. The content of necrotic substances in the synovial fluid was determined after precipitation of proteins with 5% perchloric acid on a spectrophotometer at a wavelength of 260 and 320 nm against perchloric acid. The difference in optical density (Eλ260-Eλ320)*10 corresponds to the value of the value of necrotic substances per 1 ml of synovial fluid [13]. Digital material processed by the method of variation statistics.

III. Results and Discussion

Studies have shown that in the synovial fluid of victims with a knee joint injury and post-traumatic hearthrosis, the content of AMW and necrotic substances varies widely (AMW - from 0.256 to 0.440 U/ml and necrotic substances from 1.19 to 2.73 U/ml), averaging 0.350±0.013 U/ml and 1.880±0.101 U/ml (Table 1). This was due to the heterogeneity of the examined patients, the severity of damage to the knee joint.

In this regard, we compared the indicators of AMW and necrotic substances with the data of arthroscopy of the knee joint. At the same time, the severity of inflammation was taken into account with an assessment of damage to the intra-articular structures, cartilage, synovial membrane, hemarthrosis volume. Depending on arthroscopic picture of knee joint and level of necrotic substances in the synovial fluid, patients were divided into 3 groups. Values up to 1.5 E/ml were assessed as a normal, with minimal signs of inflammation, no damage in intra-articular structures (menisci, cartilage, ligaments), edema of the synovial membrane, small volume of hemarthrosis (1st group). Values in excess of 1.5 E/ml, but below 2 E/ml was as a sign of inflammation in an affected joint, corresponding to isolated meniscus injury, ligaments, cartilage damage – according to Bauer and Jackson (1988) type I-III, moderate hemarthrosis (2nd group). Values over 2.0 E/ml were a sign of pronounced inflammatory process with progressive course that suitable to severe injury, with simultaneous damage of several intra-articular structures, hematoma of synovial membrane, the presence of severe chondral and subchondral injuries with cartilage damage. According to Bauer and Jackson (1988), it was appropriate to type IV, with the formation of free bodies inside the joint cavity (3rd group). The distribution of patients into groups showed that only 3 victims had no signs of inflammation and damage to the joint, 11 injuries had arthroscopically isolated injuries and 6 patients had severe injuries of the knee joint.

Table 1: Content of AMW and necrotic substances in synovial fluid of patients with a knee joint injury, M±m

Groups	Quantity	Medium-Weight Molecules, E/ml	Necrotic Substances, E/ml
Overall	20	0,350±0,013	1,880±0,101
1st group (from 1,5 E/ml)	3	0,289±0,019	1,333±0,081
2nd group (1,6-2,0E/ml)	11	0,338±0,015	1,708±0,051
3rd group (up to 2,0 E/ml)	6	0,403±0,014	2,493±0,063

Detailed analysis of AMW indicators and necrotic substances in the synovial fluid of the knee joint showed that the content of AMW ranged from 0.256 to 0.322 U/ml, averaging 0.289±0.019 U/ml. While the level of necrotic substances varied within narrow limits (1.19–1.47 U/ml), averaging 1.333±0.081 U/ml. Arthroscopically, any breaks of meniscus, cartilage damage, or ligaments were not identified in this group of patients. Only 1 patient was diagnosed with a contusion and hematoma of the body of Hoff and a hematoma in the synovial membrane, as well as hemarthrosis with small volumes of fresh blood poured out (33.33±3.33 ml).

In 2nd group patients, the level of AMW varied from 0.276 to 0.422 U/ml, averaging 0.338±0.015 U/ml. The content of necrotic substances ranged from 1.52 to 2.00 U/ml, making up 1.708±0.051 U/ml. Arthroscopically, there were observed in 27.3% of cases complete and in 72.7% of the partial meniscus gap, in the main first zone. According to the classification of Bauer and Jackson (1988), lesions of cartilage were shown I-III degree, incomplete rupture of ligaments and PKS, contusions of Hoff's body and in 54.5% of cases with hematomas with fresh blood of 177.27±25.30 ml.

In the 3rd group there were 6 patients. Indicators of AMW in synovial fluid varied within 0.345-0.440 U/ml, making up 0.403±0.014 U / ml, necrotic substances were from 2.30 to 2.73 U/ml, making up 2.483±0.063 U/ml.

Arthroscopically, all patients of this group were found to have a complete rupture of 3 zones of meniscus, damage to the 4th degree cartilage, complete rupture of the ligaments (combination of damage to the ACLR and medial collateral ligament (MCL). Bruises and hematomas of van't Hoff's body, the synovial membrane with hematomas and bleeding vessels, the presence of fresh blood with clots was detected in a volume of 368.33±14.47 ml.

As can be seen from the above data, biochemical indicators of synovial fluid indicated the presence of significant damage in the knee joint. However, it should be said that, in contrast to the content of AMW, mainly reflecting the increased proteolysis at the site of damage, the level of necrotic substances largely (completely) coincided with the degree of damage to the structural components of the knee joint. In our opinion, this is due to the fact that necrotic substances are products of deep destruction of cells of the body and represent a pool of components of the breakdown of nucleic acids that are able to absorb light in the ultraviolet region of the spectrum. According to the literature, the level of necrotic substances increases during inflammatory and destructive processes and is used as a marker for endotoxicosis processes. In studies taking into account the above, we analyzed the postoperative period in the patients we examined. Studies have shown that in the group of patients with a low level of necrotic substances in the postoperative period there was no development of complications. In the second group with the level of necrotic substances in the range of 1.6-2.0 U/ml in 45.4% of cases, mild inflammatory reactions developed, which were treated accordingly. The values of necrotic substances in these patients corresponded to 1.8-2.0. In the third group of victims, the values of necrotic substances exceeded 2.0 U/ml, which was predicted for a complicated course of the postoperative period, and therefore these patients were treated accordingly.

On the basis of the obtained data, we analyzed the diagnostic specificity of determining the content of necrotic substances, this indicator was 89.5%, which indicates its high predictive efficiency.

IV. Conclusion

1. In patients with damage to the knee joint, the content of AMW increases in the hemosynovial fluid, the severity of which coincides with the arthroscopic picture of the damaged joint.
2. Determination of necrotic substances in synovial fluid is a prognostic marker of severity of damage to structural components of the knee joint. Diagnostic efficacy was 89.5%.
3. The content of necrotic substances in hemosinovial fluid predicts early, preclinical diagnosis of post-traumatic osteoarthritis of the knee joint.
4. The use of a biochemical marker not only diagnoses the severity of damage to the knee joint, but also predicts the course of the postoperative period.

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