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CONTENTS

THE ROLE OF BLOOD COAGULATION FACTORS AND HYPERURICEMIA IN THE DEVELOPMENT OF CARDIOVASCULAR EVENTS IN PATIENTS WITH OSTEOARTRITIS

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ABSTRACT
Inflammation plays an important role in the pathogenesis of osteoarthritis. The study of blood coagulation markers (number of platelets, mean platelet volume, fibrinogen, D-dimer, antithrombin III, C-reactive protein, uric acid) was conducted in patients with osteoarthritis in combination with hyperuricemia and its ability to increase the risk of negative cardiovascular events. This study included 50 patients (40 men and 10 women) suffering from osteoarthritis of the knee joints. The average age of patients was 59.5±3.6 years. Patients were divided into 3 groups: group 1 – patients with osteoarthritis; group 2 – patients with osteoarthritis in combination with hyperuricemia; group 3 – control group of practically healthy patients. In patients with osteoarthritis in combination with hyperuricemia, the above-described indicators contribute to an increased risk of development of negative cardiovascular events. Therefore, there is a need for monitoring these indicators in this group of patients.

Introduction. Osteoarthritis (OA) is the most common form of joint disease [12]. Since OA is initiated by mechanical stress on cartilage, its progression depends on cellular and biochemical factors, including activation of chondrocytes and secretion of inflammatory mediators [3]. Cytokines such as interleukin (IL)-1β play an important role in the pathogenesis of OA, stimulate the production of metalloproteinases and adversely affect the survival of chondrocytes [4]. At present, there are no reliable biochemical risk markers and the prognosis of clinical progression of OA, although research in this area is carried out [2, 10].

A limited number of studies examined the possible relationship between hyperuricemia and OA. In high concentrations, uric acid (UA) may crystallize as monosodium urate (MSU), stimulating NLRP3 inflammasome and contributing to the production of IL-1β. Crystal aggregates MSU (tophus) can also directly damage the cartilage. Perhaps, these or other mechanisms, not yet defined, could contribute to the development of OA. Thus, even in the absence of gout, elevated UA levels can have a negative effect on cartilage [4].

Formation of secondary changes of cartilage tissue during gout in the form of OA is directly related to the definition of the role of the inflammatory component in the development and progression of the degenerative-dystrophic process (Li-Yu J et al., 2001). It was shown that MSU crystals that are presented in the synovial fluid stimulate the synthesis of pro-inflammatory cytokines monocytes and synoviocytes cytokines such as FNP-α, IL-6, IL-8. The latter, in turn, causes the development of chronic synovitis, inflammation of periarticular tissues and contributes to the gradual destruction of cartilage (Inokushi T et al., 2006). Increased synthesis of IL stimulates catabolism of the collagen matrix, enhances the synthesis of enzymes and degrades cartilaginous tissue, which leads to the development of secondary OA (Inokushi T et al., 2006).

It is believed that one of the key mechanisms of inflammation in OA is the activation of thrombin via a plasminogen activator inhibitor (PAI-1). It is known that thrombin takes part in the activation of platelets and endothelial cells, stimulates the deposition of fibrin, which promotes adhesion and leukocyte migration to the inflammation zone [1].

Another component of the pathological process is the specific proteolytic enzymes. In the destruction of joints in OA plasmin directly or indirectly destroys the extracellular matrix [6] and activates matrix metalloproteinases [9], which cause carotid erosion with OA [6].

Actual questions remain the definition of certain markers to characterize the course and severity of OA, as well as the study of the relationship between OA and cardiovascular diseases, their common risk factors and the main pathogenetic mechanisms. The optimal monitoring strategy for such patients in the guidelines and recommendation is not disclosed to the end.

The aim of the study was to evaluate the markers of blood coagulation in patients with OA, which contribute to the risk of developing negative cardiovascular events.

Methods. This study included 50 patients (40 men and 10 women) suffering from OA knee joints. The average age of patients was 59.5±3.6 years. The duration of the disease on the OA was 7.8±1.7 years. Diagnosis of OA was established according to the clinical and radiological criterias of the American College of Rheumatology. Patients were divided into 3 groups: group 1 – patients with OA; group 2 – patients with OA in combination with hyperuricemia; group 3 – control group of practically healthy patients. It was conducted a study of laboratory parameters: the number of platelets, the mean platelet volume (MPV), the level of fibrinogen, D-dimer, antithrombin III (ATIII), C-reactive protein (CRP), UA. Statistical processing of the study results was conducted with the using of a package STATISTICA 6.1.

Results. The arterial hypertension and coronary heart disease are most often discovered in patients with OA. It is important to note that the increased prevalence of cardiovascular diseases in OA can affect the options and outcomes of patients' treatment. In the 2nd group of patients, more than in the 1st group, high prevalence of diabetes mellitus, hypercholesterolemia and obesity were recorded in comparison with the control group. According to the study, it was found that the lowest MPV values were recorded in the second group of patients compared to the control group. Correlation between MPV and CRP was found, which testifies to association of MPV with inflammatory and cardiovascular diseases.

The effects of platelets that play an important role in inflammation and thrombogenic situations are still unknown. It can be assumed that the platelets release a large number of local inflammatory cytokines in the inflammatory area. In addition, it should be noted that due to isolated cytokines they cause activation of other inflammatory cells [2]. Thrombocyte degranulation results in the release of various growth factors and chemoattractants that affect bone metabolism [8].

The production of cytokines and the development of inflammatory process in OA, contribute to vascular damage [6] and the development of atherosclerosis, which underlie many cardiovascular diseases. According to Wang N et al., bone ischemia reduces trophic cartilage and induces multiple bone infarctions. This effect of bone ischemia is one of the potential explanations of the relationship between OA and cardiovascular disease [11].

In OA in combination with hyperuricemia, loss of chondrocytes occurs, pericellular uric acid increases, which promotes the local formation of crystals at the microscopic level [4]. The latter may, to a certain extent, be reflected in the process of blood clotting. OA is more common among patients with hyperuricemia. It was in these patients that the increased level of fibrinogen was determined by 30%, D-dimer by 18%, and decreased level of AT III by 20%. The level of blood coagulation factors was also affected by the presence of obesity and age. The accumulation of fibrinogen increases the risk of negative cardiovascular events. Since hyperuricemia, in some way, contributes to the severity of OA, its effect on the activity of blood coagulation factors is not excluded.

It was found a correlation between the level of CRP and UA; between the level of fibrinogen and CRP ($r=0.31$, $p<0.01$), indicating a negative influence of the inflammatory process and hyperuricemia on the development of cardiovascular events.

Conclusion. In patients with OA in combination with hyperuricemia, indicators such as the MPV, fibrinogen, AY III, CRP and UA, increase the risk of developing negative cardiovascular events. Therefore, there is a need of monitoring these indicators in this group of patients.

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