Volume-11| Issue-2| 2023 **Research Article**

УДК 615.825.1: 616.72-002.08

MODERN VIEWS ON THE FORMATION AND CLINICAL ASPECTS OF OSTEOARTHRITIS

https://doi.org/10.5281/zenodo.7618535

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Received: 07-02-2023
Accepted: 08-02-2023
Published: 22-02-2023

Abstract: Sufficient understanding of the prevention of consequences and complications that may occur in patients with osteoarthritis through the use of non-medication and medication measures, which are carried out early and rationally, has been given.
Keywords: Osteoarthritis, Osteoporosis, mTOR gene, Arthroscopy, synovitis

OSTEOARTRITNING SHAKLLANISHI VA KLINIK JIHATLARIGA ZAMONAVIY QARASHLAR

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Received: 07-02-2023
Accepted: 08-02-2023
Published: 22-02-2023

Abstract: Osteoartritga чалинган беморларнинг erta va ratsional amalga oshiriladigan nomedikamentoz va medikamentoz chora tadbirlarini qo‘llash orqali unda yuz berishi mumkin bo‘lgan oqibatlar va asoratlarning oldini olish to‘g‘risida yetarlicha tushunchalar berilgan.
Keywords: Osteoartrit, Osteoporoz, mTOR geni, Artroskopiya, sinovit.

СОВРЕМЕННЫЕ ВЗГЛЯДЫ НА ФОРМИРОВАНИЕ И КЛИНИЧЕСКИЕ АСПЕКТЫ ОСТЕОАРТРОЗА.

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Accepted: 08-02-2023
Published: 22-02-2023

Abstract: Дано достаточное представление о профилактике последствий и осложнений, которые могут возникнуть у больных остеоартрозом, за счет применения немедикаментозных и медикаментозных мероприятий, которые проводятся рано и рационально.

Keywords: Остеоартрит, остеопороз, ген mTOR, артроскопия, синовит.

Many scientific researchers believe that the pathogenesis of osteoarthritis (OA) is a polyetiological disease characterized primarily by degenerative-destructive processes in the cartilage of the joint. Enough concepts have been formed about the prevention of consequences and complications that may occur in OA through the use of non-drug and drug measures, which are carried out early and rationally. In addition, the achieved treatment methods provide an opportunity to reduce the patient's chronic pain syndrome, synovitis, deformation and disfigurement of the joints, reduce the need for endoprosthetics, coordinate mental-anxious and sleep disorders, depression, and improve the patient's quality of life. However, the daily increase in the prevalence of OA among the population, its tendency to chronicity, irreversible deterioration of the joints and the formation of ankylosis remain problems of this disease, not only medical, but also socio-economic. determines the importance. This has led to many opinions and discussions about the pathogenesis of OA and its nature, prompting the implementation of new diagnostic methods, epidemiological, clinical and molecular-genetic studies.

According to experts of the World Health Organization (WHO), OA is the number one cause of disability in the population over 60 years of age in almost all countries of the world, and approximately 1/10 of the world's population is affected by this disease. Therefore, primary OA is the most common nosological unit included in the XIII class of the 10th revised International Classification of Diseases. Therefore, issues related to the problem of OA are of serious importance for medicine and society as a whole. At this point, OA manifests itself clinically in the population over 40 years of age and the same working capacity is preserved, limiting the functional capabilities of millions of people and causing early disability. Epidemiological analyzes presented in recent years show that a quarter of a billion people in all countries have knee OA, and this figure is about 4% of the total population. In the developed countries of the European Union alone, the number of people suffering from OA is officially recorded as about 100 million. At this point, modern experts say that these indicators are inevitably higher in a real clinical situation. Consequently, US epidemiologists cite figures that show that nearly half a billion people have OA, almost half of whom are over the age of 65. It should be said that OA is now second only to diseases of the cardiovascular system in terms of early loss of the patient's ability to work and disability indicators. In addition, in the scientific research works of many scientists, it has been studied that

the occurrence of OA and the acceleration of the growth rate are directly related to the durability of the average life expectancy of the population and the increase in the indicators of the body weight index. It is known that OA primarily damages high-load joints (knee and hip) and causes a relatively early decrease in the patient's quality of life and work capacity. Although today, taking into account that OA is more clinically manifested in the elderly population, the relevance of the problems related to the pathogenesis of OA mainly in young age determines that in all countries, the elderly population retains significant work capacity and high social activity. In addition, one in four patients suffers from a decrease in self-confidence, social adjustment disorders, depression due to tensions in family relationships, isolation, and a state of being unwanted by society.

The development and manifestation of the disease in OA consists of the participation of a complex of pathological mechanisms. According to the modern interpretation, OA is characterized by damage to joints caused by cellular stress and micro- and macroinjuries in the extracellular matrix. These changes activate the pathological compensatory regeneration processes and trigger anti-inflammatory immune reactions, on the basis of which the subsequent development of osteophytosis and structural changes of the bone system occur.

The gonarthrosis is common among the population and is the leading cause of loss of working days and disability of patients. In the disease, joint swelling, changes in the subchondral bone and subsequent remodeling of the developing bones, osteophytes and subchondral sclerosis cause a decrease in the function of not only the knee joint, but also the musculoskeletal system. The medical and social-economic importance of OA disease is explained by the prevalence of the disease, its chronic course, the negative impact on the quality of life and health of patients, and the high cost of treatment and rehabilitation procedures. Also, in the form of polyosteoarthrosis with damage to many joints, more damage to the joints of the hands and paws, combined with a severe clinical course, creates a state of aesthetic discomfort in patients and reduces their quality of life. causes a decrease. Compared to other joint damage, patients with polyosteoarthrosis are more distrustful of medical treatment. In the joints affected by OA, there is a change in the extracellular matrix in the articular cartilage, and in the pathogenesis of the disease, cartilage destruction, re-ossification, and synovial inflammation are observed. The pathogenesis of OA lies in the disruption of the molecular structure of the hyaline matrix. As OA progresses, the tendon softens and loosens as a result of degenerative processes. In it, cracks appear that stretch to the bones . The articular surface of the bone is not protected from uneven mechanical stress due to the destroyed cartilage tissue. Zones of dynamic overload appear in the subchondral bone, which leads to a violation of the redistribution of

microcirculation. It contributes to subchondral osteosclerosis, changes in the surface of the joint, the appearance of bone-joint growths - osteophytes on the edges. Synovitis plays an important role in the pathogenesis of OA. Synovitis is morphologically characterized by proliferative and exudative reactions. It is based on the fact that infectious and autoimmune diseases in young people can lead to the development of synovitis in the knee joint.

In determining the diagnosis of osteoporosis, attention is paid to the pain in the bones of the back and limbs, the limitation of physical activity, the level of the risk of bone fractures, the level of skeletal deformation and gait disturbance as a result of bone fractures, which are important for the disease and the patient. The risk of developing osteoporosis was determined using the "Osteoporosis International Foundation" questionnaire when collecting anamnesis from suspected osteoporosis patients. When one or two questions are answered positively, laboratory-instrumental tests are conducted. From the laboratory indicators, alkaline phosphatase activity (p-nitrophenylphosphate hydrolysis method), total calcium (colorimetric method) and phosphorus amount (ultraviolet test) are determined in blood serum. Since early OA is more soft tissue damage and most inflammatory, osteoporotic and dystrophic processes develop in them, it will not be possible to detect these changes in X-ray examinations. In determining such changes, determining peripheral and hormonal indicators of calcium-phosphorus metabolism, conducting MRI, arthroscopic, densitometric examinations will be of diagnostic importance. In determining the radiological degree of OA disease, the radiological classification proposed by Kellgren (1957) and supplemented by Leuquesne (1982) is used. In relation to radiological examinations, arthroscopic examinations are important, and in patients with initial pain in the joints, even when radiographic signs are not evident (Kellgren and Lawrence grade 0), arthroscopic examinations according to the Outerbridge classification II and even III degree of OA disease is determined. The condition of the menisci and ligaments of the joints also plays an important role in the development of OA. Damage to the menisci accelerates cartilage degradation. MRI and arthroscopy allow to determine damage to the tendons and menisci. Joint USD method helps in early detection of destructive changes. This method examines the structure of affected joints, the state of the joint capsule, the structure of bones, the tendons and ligaments around the joint, the state of muscles, veins, tumors in the joint, synovial cysts, allows to determine erosions in the joint, inflammatory process, fluid volume in the joint cavity, condition of nerve fibers and vessels. USD does not harm healthy tissues, there are no contraindications. This method can determine the effectiveness of treatment. Magnetic resonance imaging examination is the method of choice when the musculoskeletal apparatus, menisci are involved in the process. MRI

examination allows to identify defects in the joint, degenerative changes, inflammatory zone, volume of fluid, fracture, tumor, cyst, protrusions, disorders of blood circulation and innervation in the joint. Arthroscopy is a method of endoscopic examination performed in traumatology and orthopedics dispensary. Arthroscopy is used for early detection of OA. Changes in the ankle are detected even in cases where there are no radiological signs of the disease. The condition of the knee joints and the general condition of the patients were studied based on the results of the questionnaire, the data of radiographic examination of the joints and the VAS indicators of pain. It has been shown that increased bone mineral density occurs in severe forms of the disease, and in particular, increased density of the femoral head can lead to the development of knee OA. Osteochondrosis of the cervical spine causes severe pain in the shoulder-scapular region based on clinical and radiological examinations. Averkiyeva Yu.V. et al., (2020) determined the mineral density of the femoral joint and lumbar vertebrae in 124 female patients with knee and hip OA. Osteoporosis was detected in 28% of patients, and osteopenia in 41% of patients. The prevalence of osteoporosis among 60-74-year-olds was 20%, and 38% among 75-90-year-olds. Increasing X-ray stage of OA disease corresponded with decreasing mineral density of the femoral neck.

It is important to note that the molecular mechanisms involved in the development of OA have been of interest to discover new pathways and develop new strategies for disease modification. Although the genetic factor has not been fully studied, it has been proven that defects in the structure of connective tissue (changes in collagen fibers) cause disorders of cartilage and bone metabolism. Among the obvious risk factors, genetic (hereditary) obesity leads to rapid and early development of the disease. Osteoarthritis is known to occur more often in people with a genetic predisposition. It is noted that osteoarthrosis and pyrophosphate arthropathy diseases are passed from generation to generation in an autosomal dominant type, and several children in the family can be affected by these diseases. At present, little attention is paid to the study of polymorphic genes responsible for the body's immune response in secondary osteoarthrosis (especially when it occurs together with RA and gouty arthritis), and there are insufficient studies in this area in primary OA. Studying the processes of gene expression related to cell proliferation, apoptosis, autophagy serves to detect OA disease in the stages before clinical development, makes it possible to determine the clinical course and consequences of the disease.

Genetic and epigenetic mechanisms underlie the pathophysiology of OA. At present, information has been gathered that methylation of DNA and microRNA molecules is the genetic basis of OA disease. However, most of these data were obtained in the late stages of the disease and were not used as early diagnostic

markers. A number of scientists have studied the molecular mechanisms of pain regulation in osteoarthritis and have shown that the expression of pain at various levels is controlled at the level of the mTOR gene system. The mTOR gene system is involved in controlling metabolic processes in the gut. The presence of MMP9 and TIMP1 genes in different proportions in the mTOR gene system provides pain with different intensity. TGFβ1 and VEGFA genes in the mTOR gene system improve tissue regeneration and reduce pain intensity.

Increased activity of the mTOR gene activates this gene through changes in many intracellular (growth factor, adenosine triphosphate, oxygenation, autophagy) and extracellular (glucose, amino acid, lipid, hexosamine metabolism) signals. causes damage to the uncle. Alterations of the mTOR gene in the blood show heterogeneity in the progression of joint pain and synovitis in OA and warrant a differential approach to treatment.

Cytokine imbalance plays an important role in the pathogenesis of OA. Cytokines are known to control hemopoiesis, inflammation, immune component cell growth and formation. In OA, the levels of interleukin-1b and interleukin-4 are normal, while the levels of interleukin-8, interleukin-10, and tumor necrosis factor-α increase in the late stages of the disease. An imbalance of these cytokines is indicative of severe OA disease.

TGF-β1 plays an important role in bone regeneration, that is, it strongly stimulates osteoblastic bone formation, participates in differentiation and differentiation of osteoblasts. During chondrogenesis, TGF-β1 is the main inducer of mesenchymal stem cell condensation. TGFβ1 signals further increase chondrocyte proliferation and lead to chondrocyte hypertrophy, stimulating synovial tissue fibrosis, fibroblast proliferation, and collagen type I and type II deposition.

In recent years, there have been significant changes in the views of scientists about the etiopathogenetic aspects of primary OA. For example, for a long time, in the course of OA, the changes in the ankle, the narrowing of the joint space, were given priority, while the SXS and other structural changes of the joint were treated as secondary important processes. However, at present, the state of SCS and the fact that pro-inflammatory cytokines (IL-1, TNF- α) have one of the leading positions in the pathogenesis of OA are presented in the scientific literature, and in a number of studies conducted in recent years, the composition and quality of SCS There are reliable data on the importance of changes (disorders in bone composition, increased breakdown and slow recovery), as well as bone mineralization in the pathogenesis and development of OA. In these processes, aspects related to the development of inflammatory-degenerative changes in

various structures of the joint based on the effect of pro-inflammatory mediators, acceleration of chondrocyte apoptosis were also studied .

The scientific views that the chronic low-grade inflammatory process takes a central place as an important factor in the pathogenetic stages of OA is attracting more and more scientific and practical interest among modern researchers today. Consequently, in OA, daily static and dynamic loads create "mechanical stress" in the joint and lead to degenerative adaptive remodeling in all its structural structures, and chondrocytes, osteocytes, synovial fibroblasts, as well as extracellular matrix elements are also involved in this process . Damaged cells and extracellular matrix elements in this process serve as the basis of DAMP (damage-associated molecular pattern - molecular fragment caused by damage), a large number of biologically active substances are released, "inflammatory response reaction" and cell activation occurs. Factors such as stable and irreversible structural and biomechanical changes developed under the influence of mechanical stress in the cellular structures of the joint play an important role.

Metabolic syndrome (MS) and obesity directly affect not only the formation and development of OA, but also its exacerbation. Recent research has shown that the need for knee arthroplasty in OA patients increases by 35% for every 5-unit increase in body mass index. Although the true pathogenetic mechanisms of the relationship between MS and OA have not been fully elucidated, the presence of MS in OA has been shown to serve as a constant source of inflammatory activity. In this regard, on the one hand, the hormones produced by adipose tissue (leptin, adiponectin, apelin) play an important role, on the other hand, due to the fact that the mass of adipose tissue is in a state of hypoxia, adipocyte cells regularly undergo systemic apoptosis and in this process, the expression of "genes associated with hypoxia" such as HIFIa, HIF2a, which activates the processes of angiogenesis and fibrosis and serves as an inflammatory inducer, is important. According to scientific data, inflammation and apoptosis of chondrocytes occur with the active participation of all components of MS (overweight, increased blood glucose concentration, dyslipidemia, arterial hypertension (AG), insulin resistance) in the pathophysiological processes of OA. Pathogenetic aspects of OA and MS Taking into account the interrelationship, a number of researchers have noted that early detection and correction of individual components of MS have a positive effect on the progression of OA. From this point of view, medicinal agents whose pharmacological effects are aimed not only at the treatment of OA, but also at the elimination of existing metabolic disorders are of scientific and practical interest. For example, in the treatment of MS and obesity-related OA, the specifics of using diacerein in the therapy of OA continue to be explored by modern researchers.

Thus, the prevalence of OA among the population, the high incidence rate of this disease among people of working age, and the constantly worsening clinical course make the disease one of the medical and social problems. The specificity of the clinical features of OA and the additional comorbidity situation of the joint syndrome, which progresses continuously, require a new approach to this disease, and this creates the need for coordination in diagnosis and treatment.

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