ISSN NO: 2770-2936
Date of Publication:06-07-2022

Metabolic and Immunological Aspects of Osteoarthritis

Ramazanova Nigora Asrarovna
Postgraduate student of the department
Propaedeutics of internal diseases No1
Tashkent Medical Academy
leoness555@mail. ru

Annotation: The review article highlights the scientific works of foreign scientists on metabolic, immunological causes and pathological mechanisms of osteoarthritis, which is becoming younger and an urgent problem among arthrolgic diseases in the elderly, leading to early disability and increasing economic problems.

Keywords: Osteoarthritis, metabolic disorders, obesity, immunology, biomarkers, phenotype, leptin, adiponectin, IL-1, IL-6.

Osteoarthritis (OA) affects 240 million people worldwide [1] and is one of the ten most disabling diseases in developed countries.

The most common form of arthritis is osteoarthritis (OA). In the Global Burden of Disease 2010 study, hip and knee OA ranked 11th in global disability (Cross et al., 2014). The prevalence of OA will increase in parallel with the increase in the number of people aged 60 years and older and the increase in obesity worldwide. Cohort studies have shown that after aging, obesity and metabolic disorders are the main risk factors for developing OA (Aspden et al., 2001 ; Felson et al., 1988). Conversely, OA is a risk factor for metabolic syndrome and cardiovascular disease, suggesting that effective treatment of OA may prevent or delay the development of a large number of comorbidities (Haugen et al., 2013; Prior et al., 2014) [2].

There is growing evidence that there are different phenotypes of OA, reflecting different mechanisms of pathology. In 2016, evidence from six potential clinical phenotypes was presented in the literature: those occurring with chronic pain; with inflammation; with metabolic syndrome; bone and cartilage metabolism; mechanical overload; and minimal joint involvement [3]. These researchers subsequently examined the prevalence of these phenotypes in the OA Biomarker Consortium (OAI/FNIH) Foundation dataset of the National Institutes of Health [4]]. Another review focused on molecular/mechanicalendotypes, particularly those associated with inflammation (characterized, for example, by c-reactive protein and interleukin-6), bone (e.g., c-terminal collagen telopeptide I [CTX-I]), metabolic syndrome (e.g., adipokines, advanced glycation end products), and aging (markers of aging) [5]]. Recent efforts have been made to standardize the conduct and reporting of phenotypic studies in OA [6], in which it has been noted that phenotypes are "subtypes of OA that have various underlying pathobiological and pain mechanisms and their structural and functional consequences" [7].

Metabolic syndrome is a term encompassing a complex of hormonal and metabolic disorders, a serious medical and social problem of our time. Due to its prevalence among the adult population, MC is called the "syndrome of the new era" [8]. For the first time in 1988. J.M. Riven formulated the concept of MC as "X-syndrome". Thus, in 1989, abdominal obesity was identified as the most important etiological factor in the formation of insulin resistance, and obesity, especially in the upper body, increased glucose tolerance in hypertension. Thus, this combination is most indicative for increasing mortality from cardiovascular diseases [9].

Adipose tissue is a type of connective tissue made up of blood vessels, collagen fibers, fibroblasts, and an extensive network of the immune system surrounded by lipid cells called adipocytes [10]. According to the classification, adipose tissue is divided into two types: white and gray. They are characterized by different anatomical localization, structure and functions. Adipose tissue produces many biologically active substances, among which an important role is played by adipokines and adipocytokines [11].

More than 50 adipokines are known, including leptin, adiponectin, resistin, visfatin, etc., which secrete anti-inflammatory cytokines, such as tumor necrosis factor a (TNFa), interleukin 6 (IL6), inhibitor 1 of the

ISSN NO: 2770-2936
Date of Publication:06-07-2022

plasminogen activator and others. Adipokines are biologically active substances produced by white adipose tissue and have a pleiotropic effect. They are involved in a wide range of metabolic processes, including not only carbohydrate x and fat metabolism, but also modulationand immune and inflammatory responses. Adipokines contribute to the chronic inflammatory process and interact with other cytokines, which together enhance degenerative processes in the joints [12]. Due to synergistic relationships with IL1, adipokines can enhance catabolic processes in cartilage and increase the synthesis of pro-inflammatory mediators in joint tissues [13]. Thus, obesity, cardiovascular lesions and other pathogenetic metabolic disorders are associated with OA, which can be viewed as a systemic disease.

Adipokine levels in patients with OA were significantly higher than in the control group. In particular, high levels of adiponectin and leptin areassociated with female sex and high BMI [14].

Odin of the main adipokines involved in metabolic processes in OA is Leptin, it is produced by white fat cells. And its circulation directly depends on the amount of fat in the body. It is not only the main regulator of body weight, but also suppresses appetite, stimulates energy expenditure using the receptorof the hypothalamus. Leptin production is regulated by hormones, inflammatory mediators (such as TNFa, IL1, IL6) and writing techniques. [15,16]. Increased production of leptin leads to an increase in the levels of alkaline phosphatase, osteocalcin, collagen type I and variable growth factor b1, which in turn has a positive effect on the dysregulation of osteoblasts [17]. In patients with OA, leptin is found in considerable quantities in the synovial fluid and in the synovial membrane of the knee joints (CS) [18]. In a 10-year study at the University of Michigan, the relationship of leptin levels with radiographic signs of OA in women was found. The authors identified that an increase in leptin levels by 5 ng / ml in the blood serum progresses radiographic signs of OA by 38% and increases the risk of OA COP by 31% [19].

Adiponectin broad is associated with a range of inflammatory components in diseases (cardiovascular disease, type 2 diabetes, MS and OA) [20]. But still, its role in OA remains not fully understood. In the study, E. Distel et al. [21], an increase in adiponectin production has been detected in OA and MC. Infrapatellar adipose tissue (IHT) of OA patients not only consists of adipocytes, but in large quantities has macrophages, lymphocytes and granulocytes. It is able to produce and produce a large amount of leptin and adiponectin, synthesize inflammatory mediators (TNH, IL6) in high concentrations, distinguishing from subcutaneous fata [22]. To all this, IHT in OA is very well innervated with small C-fibers of neurons, which are contained in neuroinflammatoryx mediator ah and vasodilatorah - substance P, it not only forms sensations of pain, but also directly affects various cells of the immune system, provoking the synthesis of pro-inflammatory cytokines (IL1, FNOα) [23]. The secretion of leptin in the IHT is sufficient to produce MMP1 and MMP13 in chondrocytes thatwould help maintain chronic inflammation [24]. In studies by M. Rai, L. Sandell, it is also proved the important role of IHT as a source of adipokines, cytokines and chemokines, in catabolic and pro-inflammatoryprocesses [25]. As we understand it,obesity is a mild inflammatory process, causing systemic metabolic dysfunction. In obesity OA, the production of adipokines with pro-inflammatory functions increases, which contributes to the progression of the disease [26].

Recent evidence suggests that adipokines produced by white adipose tissue may provide a link between obesity and OA, which explains the high prevalence of OA among obese and overweight people (Scotece & Mobasheri, 2015). In their review, Kluzek et al. discussed the role of leptin, resistin, and cystfatin as key mediators of catabolic pathways associated with cartilage degeneration. The paper looks at adipokines as prognostic biomarkers of early post-traumatic osteoarthritis of the knee joint (Kluzek et al., 2015b) [27].

Biomarkers help healthcare professionals diagnose disease at an early stage, observe its course and monitor how well new or existing treatments work. Biomarkers include:

- Biomarkers that help diagnose disease
- Biomarkers that help predict disease
- Biomarkers that allow you to assess the physical condition of the patient.

In 2006, the group Bauer et al., (2006) published a paper presenting the characteristics and classification of OA biomarkers.

The diagnosis of OA is usually based on clinical and radiographic changes that occur very late and have low sensitivity for monitoring the progression of the disease (Rousseau & Delmas, 2007, Rousseau & Garnero, 2012). , in addition to biomedical imaging (Rousseau & Garnero, 2012) [28].

ISSN NO: 2770-2936
Date of Publication:06-07-2022

To date, there are many barriers to theidentification of biomarkers that reflect OA: Gistochemical data are not associated with clinical signs such as pain and function. First of all, it has been shown that inflammation in OA is not only local, but also systemic, which complicates standard studies. Various factors of systemic inflammation are immeasurable: age, genetics, diet, activity, kidney function, liver function, weight and other comorbidities and manyaboute oe.

Adipokines associated with inflammation include classic pro-inflammatory agents (IL-6, TNF-α). IL-6 produced by adipose tissue accounts for about a third of circulating IL-6 and is strongly associated with increased obesity (Proenca et al., 2014) [29].

The group of inflammatory cytokines is the most important group of compounds involved in the pathogenesis of OA. They are most responsible for the loss of metabolic homeostasis of the tissues that form the joints by promoting catabolic and destructive processes. The key role they play in the pathogenesis of OA is as a result of exposure to these compounds on most cells that are found in the joint, and the influence through intracellular signaling pathways on the production of cytokines, as well as other inflammatory compounds and enzymes. Among the many representatives of this group, the greatest importance is attached to the IL-1, IL-6. [30] .

Interleukin (IL)-1 is a cytokine that plays an important role in inflammatory responses in the context of infectionand immune-mediated diseases. IL-1 is present in the synovial tissue and fluids of patients with OA and rheumatoid arthritis. Several in vitro studies have shown that IL-1 stimulates the production of mediators such as prostaglandin E(2), nitric oxide, cytokines, chemokines, andadhesion molecules. which are involved in joint inflammation. In addition, IL-1 stimulates the synthesis and activityof matrix metalloproteinase and other enzymes involved in the destruction of cartilage in OA and RA. The effects of IL-1 are inhibited in vitro and in vivo by natural inhibitors, such as the IL-1 receptor antagonist and soluble receptors. The IL-1 receptor antagonist inhibits the action of IL-1, blocking its interaction with the surface receptors of cells. The use of IL-1 inhibitors in experimental models of inflammatory arthritis and osteoarthritis provided strong support for the role of IL-1 in the pathogenicity of these diseases. Most importantly, these results have been confirmed in clinical trials in patients with rheumatic diseases. Additional strategies aimed at blocking the effect of IL-1 are being tested in clinical trials.

IL-6 is a 184 amino acid protein [31] that has been shown in a number of studies to play a pro-inflammatory role in the pathophysiology of OA. Healthy chondrocytes produce small amounts of IL-6 without the presence of a stimulating agent [32], but when exposed to certain cytokines, including IL-1β, a key player in inflammation of arthritic joints, chondrocytes increase their production [33,34]. Similarly, TNF-α and interferon-γ also induce the production of IL-6 [35]. IL-6 inhibits the production of type II collagen in animal models [36]. In a study of 82 patients with knee joint OA, it was shown that the level of IL-6 in the synovial fluid (SF) did not correlate with body mass index (BMI), age or severity of OA (KL) [37]. In a study of patients with hip OA, the level of IL-6 in the blood serum of women was positively associated with hip JSN, but not with the presence of osteophytes[40]. Instead, in a recent study of 160 postmenopausal women conducted by Shimura *et al.[38]*, serum IL-6 levels were associated with the severity of pain in early-stage knee OA, but not in advanced stages of the disease [39,40].

The tactics used by the researchers are to influence cell transduction pathways, which are crucial for inducing the inflammatory process. Therefore, studies are underway to obtain more accurate knowledge about the action of inflammatory and anti-inflammatory cytokines.[41]

References

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5835411/
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4840279/
3. Dell'Isola A, Allan R, Smith SL и др. Выявление клинических фенотипов при остеоартрозе колена: систематический обзор литературы. BMC Musculoskelet Disord.2016 12 октября;17(1):425. [Crossref], [PubMed],[Google Scholar]
4. Dell'Isola A, Steultjens M. Классификация пациентов с остеоартрозом колена в клинических фенотипах: данные инициативы «Остеоартрит». PLoS One. 2018;13(1):e0191045. [PubMed], [Web of Science ®],[Google Scholar]