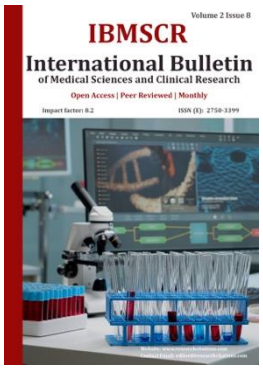

RHEUMATOID ARTHRITIS: DIAGNOSTIC AND TREATMENT ALGORITHMS

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Abstract:

Rheumatoid arthritis (RA) is a chronic inflammatory disease that mainly affects the joints, especially the joints of the hands and feet. The disease is caused by the immune system attacking itself and causing inflammation in the tissues between the joints. RA is more common in women than men and is most common in the 30-60 age group. The disease can cause joint deformity, immobility, and pain. This article provides detailed information about the causes, diagnostic methods, treatment methods, and preventive measures of rheumatoid arthritis. Modern methods such as medications, physiotherapy, and exercise are used to effectively treat rheumatoid arthritis. Early detection and proper treatment of the disease play an important role in improving the patient's overall quality of life.

Keywords: Rheumatoid arthritis, joints, immune system, inflammation, diagnostics, treatment, biologics, physiotherapy, chronic disease, pain, joint deformity.

Rheumatoid arthritis (RA) is an immune-inflammatory (autoimmune) rheumatic disease of unknown etiology, characterized by chronic erosive arthritis and systemic damage to internal organs, leading to early disability and reduced life expectancy of patients [1]. The introduction into clinical practice of new effective drugs, the so-called genetically engineered biological drugs (GEBD), inhibitors of "signaling molecules" and especially the improvement of the RA treatment strategy using standard disease-modifying anti-inflammatory drugs (DMARDs), primarily methotrexate (MTX), as well as glucocorticoids (GC), has led to a dramatic improvement in the prognosis for this disease [2, 3]. Within the framework of the Treat to Target strategy, the goal of RA therapy is not only symptomatic improvement of the patient's condition, but also achievement of clinical remission [4, 5], which reduces the risk of loss of ability to work, disability and increases the life expectancy of patients to the population level [6]. A detailed description and justification of modern recommendations regarding the treatment of RA are presented in previous publications [2, 3, 7]. According to epidemiological studies, the widespread introduction of modern RA treatment strategies into clinical practice has led to a higher frequency of remission, compared with previous decades [8, 9]. Nevertheless, many theoretical and clinical problems remain, concerning both the definition of the concept of "remission", its characteristics and types, and approaches to the optimal tactics of "symptomatic" and "pathogenetic" drug therapy at different stages of the disease, the use of which allows for rapid induction of remission and its maintenance in the long term [10]. This is associated with the heterogeneity of the pathogenetic mechanisms of RA, which is reflected in the existence of a wide range of phenotypes and endotypes of the disease and allows us to consider RA not as “one disease”, but as a clinical immunological syndrome [2, 3].

Currently, to characterize remission in RA, mainly clinical "tools" are used, allowing indirect assessment of signs of inflammation - pain and swelling of the joints, but not the

actual intensity of inflammatory damage to the synovial membrane and internal organs. Several indices have been developed to characterize the state of remission [11-13], each of which has its own advantages and disadvantages [14, 15], to a greater or lesser extent, allows for the presence of "residual" joint inflammation and completely ignores the "autoimmune" component of RA pathogenesis. For example, the values of the DAS index strongly depend on "acute phase" indicators - ESR, C-reactive protein (CRP) level [16]. This may "overestimate" the real efficacy of some drugs, such as interleukin 6 (IL6) and Janus kinase inhibitors, which have a greater effect on laboratory (ESR and CRP) than on clinical parameters (the number of painful (NTP) and swollen (SJ) joints, the general condition of patients), unlike other biologic agents [17]. Therefore, at present, according to the recommendations of the American College of Rheumatology / European League Against Rheumatism (ACR / EULAR), it is recommended to take into account the SDAI index values and the Boolean criteria to characterize remission [11, 16]. At the same time, the correct calculation of NTP and / or SJS is often difficult, has a relatively low reproducibility [18], does not allow for the detection of subclinical joint inflammation [19] and does not take into account other possible manifestations of rheumatoid inflammation (e.g., tenosynovitis). Another aspect of this problem is related to the contribution of an important component of all RA activity indices – the “patient global assessment” (PGA) indicator. In particular, there is evidence that a third of RA patients who do not have painful and swollen joints during clinical examination and who have a CRP concentration of ≤1 mg/L have PGA values >1 [20]. The condition of these patients is described by the term “near-remission” [21]. It is noteworthy that the “near-remission” state is observed significantly more often than “remission” (in a ratio of 1:1 to 1:4). It has been established that PGA may be associated not so much with “inflammatory activity” as with social, demographic, psychological and other factors, comorbidity, the presence of secondary fibromyalgia or osteoarthritis [22]. It is believed that these patients need not so much intensification of anti-inflammatory therapy to achieve remission, but rather the selection of adequate analgesic therapy, physiotherapy, and correction of psychological factors (antidepressants, etc.).

From the point of view of the clinical prospects of patients in remission, the state of "temporary", "stable", "drug-induced" (with or without GIBP) or "drug-free" clinical remission should be considered. Along with clinical remission, approaches are being developed to identify the so-called “instrumental/serological remission”: a combination of clinical remission and the absence of inflammation in ultrasound examination (US), magnetic resonance imaging (MRI) and serological signs of inflammation (normalization of ESR and CRP), as well as “immunological remission” - clinical and “instrumental/serological remission” in combination with seronegativity for rheumatoid factor (RF) and antibodies to citrullinated proteins (ACP) or documented “seroconversion” of RF and ACP [10].

In patients with RA, pain is not always caused by arthritis. It can also be associated with comorbidities, such as osteoarthritis (OA) or fibromyalgia [8]. The causes of pain in RA can vary significantly at different stages of the disease, at different levels of its activity, and among patients. The inflamed synovium produces prostaglandins, bradykinin, proinflammatory cytokines including tumor necrosis factor (TNF) α, interleukin (IL) 1, 6, and nerve growth factor (NGF) β, which sensitize peripheral nerves, contributing to the onset and maintenance of pain [9]. Synovitis is associated with changes in the expression of neurotransmitters such as γ-aminobutyric acid, substance P, calcitonin gene-related peptide, and their receptors in

the spinal cord [10]. Activation of spinal cord microglia promotes the production of TNFα, IL1, 6, which further enhances the transmission of nociceptive signals. Increased descending activation and weakened descending inhibition can lead to further pain aggravation [11]. The central sensitization zone can be wider than the area corresponding to the innervation zone of the inflamed joint, which helps to reduce the pain threshold in the periarticular tissues [12]. A decrease in the pain threshold is associated with a bad mood and sleep disturbance, characteristic of fibromyalgia. If the disease is long-standing, pain can be associated with joint damage caused by chronic inflammation or concomitant OA [13]. Structural changes developing in RA are associated with more severe arthralgia, although they alone account for only 2% of pain intensity [14]. Increased pain can be caused by psychological factors. In this case, pain has a negative impact on the psychological state of the patient [15]. The sensation of pain is a complex phenomenon that includes sensory and emotional components. Although inflammation plays a major role in its occurrence, the persistence of pain with adequate control of inflammatory activity indicates the involvement of other mechanisms in its origin. Pain is considered an unfavorable prognostic factor. High pain intensity in early RA is associated with more pronounced functional impairment one year after the start of observation [16]. RA patients describe their pain sensations differently. At the same time, the presence of aching pain in the area of the affected joints may be associated rather with inflammatory changes, burning and shooting pain allow us to think about the participation of neuropathic mechanisms and the involvement of nerves [17]. The appearance of widespread pain sensations associated with fatigue, sleep and mood disorders indicates the involvement of central mechanisms of pain perception. Pain is one of the seven indicators selected by ACR experts to assess RA activity, but the results of its assessment are not used to calculate the summary indices (DAS28, SDAI, CDAI) recommended by EULAR to determine the level of inflammatory activity in clinical practice. However, special studies have shown that pain intensity has a significant impact on the patient's overall assessment of disease activity [18]. The severity of pain sensations accounts for approximately 75% of the variability of this indicator.

Pain also has a significant impact on the physician's overall assessment of disease activity. Therefore, the patient's pain can significantly affect the assessment of RA activity and the physician's decision on the need to adjust drug therapy, which he makes in accordance with the "Treat to Target" principle.

Meanwhile, a significant proportion of RA patients are elderly people, and their joint pain may be due to the presence of concomitant OA. It should also be noted that OA often affects the joints of the hands and knees, which are included in the 28 joints examined to calculate the DAS28, SDAI, and CDAI indices. Therefore, OA-induced changes can significantly affect the number of painful joints. Thus, in a patient with RA, pain caused by concomitant pathology can seriously distort the result of assessing inflammatory activity according to the EULAR-recommended summary indices, and such an error can cause an unjustified increase in basic therapy. Therefore, effective pain suppression allows not only to significantly reduce the patient's discomfort, but also to more correctly select treatment tactics in each specific case.

Summary

Rheumatoid arthritis is a chronic disease in which the immune system attacks its own healthy tissues. Early diagnosis and appropriate treatment are essential to improve the patient's

quality of life. Modern medications, physiotherapy, and surgical interventions are effective in reducing the effects of RA and helping to ensure the long-term health of patients.

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