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Research Article

MODERN METHODS OF TREATMENT OF PATIENTS WITH ANKYLOSING SPONDYLITIS

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ABSTRACT

The review article presents modern methods of treatment of ankylosing spondylitis, including the use of both non-drug and drug therapy. Of the medical methods of treatment, a critical review of the available modern drugs, including their shortcomings, is presented. The article also points out the lack of clear recommendations for the introduction and treatment of AS patients during the pandemic, taking into account the incidence of COVID-19.

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KEYWORDS

Ankylosing spondylitis, treatments, basic antirheumatic drugs, IL-17 inhibitors.

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic HLA-B27 associated autoimmune disease characterized by damage to the spine and lumbosacral joint, resulting in its ankylosing and the development of disability in patients [3, 4]. The disease has a demographic character, its prevalence in the world averages 0.1-1.5% [17]. The disease has gender differences and is more common in men; the first onset of the disease usually begins before the age of 40 [9]. Unfortunately, according to statistics, the disease is more severe in women [2]. The disease is social in nature because it leads to early disability of the young population [23].

In recent years, therapeutic recommendations have been developed and updated in the world to improve the treatment of AS patients. in 2016, updated guidelines from Spondyloarthritis International and the European League Against Rheumatism (ASAS-EULAR) [6] were published, and in 2019, guidelines from the American College of Rheumatology/Spondyloarthritis Association of America (ACR/SAA) [26].

Treatment is recommended to combine non-drug with medication. With AS, the role of therapeutic physical exercises (exercise therapy) is very high, after which the pain syndrome, morning stiffness are significantly reduced, and the functional activity of the spine increases. Daily gymnastics is recommended with a gradual increase in its duration, it is allowed to be divided into several approaches during the day, gymnastics using weight loads is excluded [10, 16].

Non-steroidal anti-inflammatory drugs (NSAIDs), basic antirheumatic drugs (DMARDs), genetically engineered biological therapy drugs (GIBTs) are used from medical treatments. According to international recommendations, first-line drugs are NSAIDs, which are recommended to be taken without interruption, for a long period, and an additional monthly course of dual anti-inflammatory therapy is also possible. NSAIDs reduce the activity of the disease, reduce the manifestations of the disease, according to some authors, and slow down the radiological progression of the disease [6, 15].

When prescribing drugs, it is necessary to take into account the ratio of benefits and risks, but unfortunately, international organizations take into account only the benefits, ignoring the serious side effects of NSAIDs that we encounter every day in practical rheumatology. Very often, patients take NSAIDs to relieve pain, but it does not take into account that the cause of pain is associated with the presence of disease activity, this often leads to the fact that patients simply mask the symptom of pain without affecting the cause of the pain, there are also no data of these drugs on the suppression of autoimmune process

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and inhibition of key pro-inflammatory cytokines: IL17, IL23, TNF-α. International recommendations of the 2019 revision, which recommend changing the "on demand" intake to a long-term, lifelong intake, also increase the risk of such serious side effects as gastric ulcers, toxic liver damage, intestinal nephritis, increased blood pressure up to hypertensive crises, which in turn may result in myocardial infarction or stroke. In our many years of practice, unfortunately, we met many patients who took exclusively NSAIDs and this led not only to their numerous side effects, but also to the progression of the disease up to ankylosing of the spine and joints, leading to disability of patients [1].

The second line of drugs for the treatment of AS are basic antirheumatic drugs, among them only sulfasalazine showed only moderate efficacy in the treatment of the peripheral form of the disease, methotrexate and leflunamide are ineffective drugs in the treatment of AS [3]. However, we do not entirely agree with this opinion. The opinion that the appointment of sulfasalazine is ineffective and only in the peripheral form in practical rheumatology is not confirmed. The effectiveness of sulfasalazine in both axial and peripheral forms of AS was noted, which is consistent with the opinions and studies of a number of other scientists [21]. But, it should always be taken into account that the appointment of basic therapy is always a selection method and with low efficiency, some drugs are replaced by others [1].

Targeted DMARDs are a new class of drugs that inhibit Janus kinases: tofacitinib, filgotinib, and upadacitinib [22]. In a 12-week study of the efficacy of filgotinib in NSAID refractory patients, 33% showed a decrease in ASDAS activity. Upadacitinib, a jacus kinase inhibitor, was studied in a large SELECT-AXIS 1 study involving 187 patients with AS. To date, interim data have been presented by scientists, upadacitinib at a dose of 15 mg once a day showed sustained and stable efficacy for 1 year, an additional year of study is required for the final result [25]. The embarrassing part of this study is the safety of this drug, 612 adverse events were reported in 182 patients, although there are no data on serious side effects, but still the figure remains very high [1].

Preliminary data from many scientists around the world on the study of Janus kinase inhibitors in AS demonstrate their similar clinical efficacy with TNF-α inhibitors [22]. TNF-α inhibitors have shown their effectiveness for many years, a few years ago this group was the only genetically engineered drug for the treatment of AS. Scientists have proven that TNF-α inhibitors help reduce the activity of the inflammatory process according to the ASDAS and BASDAI scales, reduce the number of inflamed joints, and improve the quality of life of patients [8, 15].

However, as some patients have not responded to this group of drugs or experienced secondary resistance, the introduction of IL-17 inhibitors such as secukinumab and ixekizumab has expanded treatment options, and there are now three more drugs (bimekizumab, brodalumab and netakimab) that are undergoing various clinical stages. tests [11,12].

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IL-17 blockers have shown high and stable safety, effectiveness in reducing the activity of the disease, slowing down the progression of osteoarticular changes in the spine due to the inhibition of this group of drugs, a key pro-inflammatory cytokine that plays a role in the progression of AS [7, 13, 18, 19].

In recent publications, the results of a study devoted to the study of the effectiveness of the selective dual inhibitor of IL17A and IL17F bimekizumab were published. Studies were conducted on 303 patients with AS, patients with different dosages of bimekizumab were followed up for 48 weeks. By the end of the study, more than 60% of patients receiving bimekizumab at a dosage of 320 mg achieved ASAS40, the drug showed a rapid and sustained improvement in key indicators in AS [20].

After the appearance of IL-17 inhibitors, which showed excellent results in slowing down the radiological deterioration of AS, the issue of the effect of TNF-α inhibitors on the spine became controversial, many scientists believe that this group of drugs reduces the activity of the disease, but does not slow down the progression of AS, since it does not reduces IL-17 [14]. The phase IIIb SURPASS study will aim to address this issue, with 858 AS patients divided into three groups: the first group consisted of patients receiving secukinumab at a dosage of 150 mg, the second group 300 mg and the third group receiving adalimumab. The study will be carried out for two years and will give an answer to this controversial question, which many scientists of the world have been studying for several years [24]. Despite the high efficiency of IL-17 inhibitors, according to the recommendations of international associations, it is recommended to start treatment with genetically engineered drugs for AS with TNF-α inhibitors and, if they are not effective, switch to IL-17 inhibitors [15].

The biggest surprise was the absence of any effect from the inhibition of IL-23, which plays an important role in the pathogenesis of the IL17/IL23 axis in AS. The efficacy of ustekinumab and risankizumab in the treatment of AS has not been confirmed in a number of large cohort studies [3].

A study of the world literature showed that international recommendations for the treatment of AS are outdated and require modernization, and there are also no clear recommendations for the introduction and treatment of patients with AS during a pandemic, taking into account the incidence of COVID-19.

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