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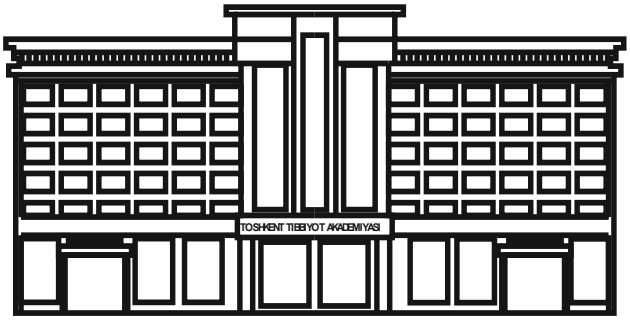

ВЕСТНИК ТАШКЕНТСКОЙ МЕДИЦИНСКОЙ АКАДЕМИИ

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METHODS OF SECONDARY PREVENTION IN PATIENTS WITH ANKYLOSING SPONDYLOARTHRITIS UNDER COVID-19

Abdurahmanova N. Mirza-Bakhtiyarkhanovna

COVID-19 ЎТКАЗГАН АНКИЛОЗЛОВЧИ СПОНДИЛОАРТРИТГА ЧАЛИНГАН БЕМОРЛАРДА ИККИЛАМЧИ ПРОФИЛАКТИКА УСУЛЛАРИ

Абдурахманова Н.Мирза-Бахтиярхоновна

МЕТОДЫ ВТОРИЧНОЙ ПРОФИЛАКТИКИ У БОЛЬНЫХ АНКИЛОЗИРУЮЩИМ СПОНДИЛОАРТРИТОМ ПОСЛЕ ПЕРЕНЕСЕННОГО COVID-19

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В статье приведенны результаты собственных исследований больных анкилозирующим спондилоартритом (АС) перенесших COVID-19. На основании проведенных исследований разработаны методы вторичной профилактики включающие раннею диагностику, а так же методы лечения АС, учитывая особенности течения COVID-19 и влияние его на данное заболевание.

Ключевые слова: *COVID-19, анкилозирующий спондилоартрит, вторичная профилактика.*

Мақолада COVID-19 ўтказган анкилозловчи спондилоартритга (АС) чалинган беморларни ўрганиш тадқиқот натижалари келтирилган. Ўтказилган тадқиқотлар асосида АС нинг иккиламчи профилактика усуллари, жумладан, эрта ташхислаш ва даволаш, шунингдек COVID-19 кечишининг ўзига хос хусусиятлари ва уни ушбу касалликка таъсирини ҳисобга олган ҳолда АС ни даволаш усуллари ишлаб чиқилди.

Калит сўзлар: *COVID-19, анкилозловчи спондилоартрит, иккиламчи профилактика*

Coronavirus disease 2019 (COVID-19), declared a pandemic by WHO on March 11, 2020, struck the whole world with the high contagiousness of the disease, the diversity of mutant strains, the polymorphic clinical picture, as well as the damage to various organs and systems [3, 7, 8, 16]. COVID-19 has a significant impact on the condition of patients, leading to the development of post-COVID syndrome, but in addition, it is especially difficult for patients with various comorbid conditions, autoimmune diseases, as well as patients taking immunosuppressants [6, 9, 11, 17, 24]. Often, in such patients, after suffering a coronavirus infection, a deterioration in the condition is observed, with the development of an exacerbation of the underlying premorbid pathology [10]. Carrying out timely therapeutic and preventive measures can prevent the worsening of the course of chronic autoimmune diseases, such as ankylosing spondylitis (AS) [14, 15, 19].

Ankylosing Spondylitis is a chronic autoimmune inflammatory rheumatic disease that primarily affects the axial skeleton, including the spine and sacroiliac joints, and is characterized by inflammatory back pain, peripheral joint involvement, inflammation of the enthesis (enthesitis), eye involvement (uveitis) and detection in more than 80-90% of cases of the genetic marker HLA-B27 [4, 5, 12]. At present, methods of therapeutic and preventive measures for patients with AS who have undergone COVID-19 have not been sufficiently developed in Uzbekistan.

The aim of our study was to develop methods of secondary prevention in patients with AS who had undergone COVID-19.

Materials and methods of research: In the period from 2020-2022, 98 patients with a diagnosis of AS were examined in the City Clinical Hospital # 3 of Tashkent city and the Multidisciplinary Clinic of the Tashkent Medical Academy. The control group was 30 healthy volunteers of the corresponding average age. The diagnosis of AS was made according to the modified New York criteria for the diagnosis of AS. The patients were divided into two groups: group I - 47 patients with AS who underwent COVID-19 and group II - 51 patients with AS who did not have a history of COVID-19 infection. The mean age of patients in group I was 37.5±3.4 years and in group II 38.8±6.1 years. Disease activity was studied using the BASDAI and ASDAS scales, functional disorders were assessed using the BASFI index, the MASES scale was used to assess pain and swelling of entheses, pain syndrome was assessed using the visual analogue scale (VAS). All patients underwent in-depth clinical, laboratory and radiological studies, testing using various scales. All patients underwent PCR, as well as ICLA tests for the presence of antibodies to COVID-19.

Statistical processing of the research results was carried out using the Microsoft Office Excel 2013, "Statisticks" application programs on a personal computer.

Research results: Clinical studies have shown that the majority of patients with AS experienced COVID-19 asymptomatically or with few symptoms, with mild or moderate severity of the disease. In most cases, the presence of an elevated titer of IgG antibodies to COVID-19 was an incidental finding for patients, while not one patient received vaccination against coronavirus infection due to a relative contraindication for AS. Studies of both groups showed the presence of both axial and peripheral forms of joint damage.

The main complaints of patients in both groups were such as morning stiffness, which was observed in 82% of patients in both groups; night and daytime back

pain was noted by 95% of patients of group I and 76% of patients of group II; joint swelling in 72% of group I, in 59% of group II.

The study of pain intensity according to VAS was 8.9±2.2 in group I and 6.6±1.4 in group II (p<0.05). Laboratory studies showed an average erythrocyte sedimentation rate (ESR) in group I 41.1±5.5 mm/h 34.4±4.1 mm/h in group II (p<0.05). The level of C-reactive protein (CRP) was elevated in both groups (23.4 ± 3.2 mg/l and 14.9 ± 5.1 mg/l, respectively), indicating a high AS activity in both groups (p>0.05).

The study of AS activity using the BASDAI scale showed an average level of 7.01±0.9 points in group I and 4.5±1.1 points in group II (p<0.05). And the study of activity on the ASDAS scale showed an average level of 4.09±1.2 points in group I and 2.7±1.2 points (p<0.02) in group II, which indicates a very high activity of the pathological process in group I and high activity in Group II (Fig. 1.).

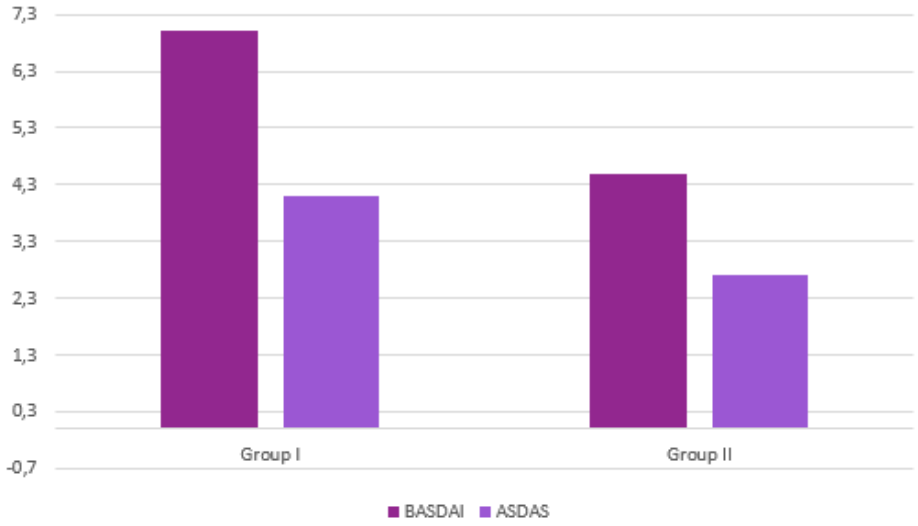

Fig.1. The level of activity according to the BASDAI and ASDAS scales in the studied groups.

When conducting x-ray studies, it was found that in 10% of patients of group I and 8% of group II, the first x-ray stage of AS was verified, in 42% and 39% stage II, in 33% and 41% stage III, in 15% and 12% respectively IV stage of sacroiliitis.

When examining blood fibrinogen, an increase in its level was revealed in patients in group I compared with group II (439.8±23.4 g/l and 378.1±18, which indicates the persistence of hypercoagulable syndrome after suffering COVID-19.

Patients of both groups in a hospital received traditional therapy including non-steroidal anti-inflammatory drugs, glucocorticosteroids (GCS) in injectable form and in the form of intra-articular injections, basic therapy including sulfasalazine (if it is intolerable or ineffective - leflunomide, methotrexate, plaquenil), gene- engineered biological preparations (GIBP) according to the recommendations of the Ministry of Health Protection of Uzbekistan. Part of the patients of the first group of GIBD were recommended blocker of interleukin-17 (IL-17) receptors - secukinumab (n=20). Secukinumab was recommended at a dosage of 150 mg as a subcutaneous injection once a week for 2-4 weeks. The remaining patients from the first group received standard treatment without secukinumab. With dynamic observation for 6 months during treatment with secukinumab, low disease activity was achieved, which persisted for 6 months. In patients who received standard treatment without secukinumab, after a slight decrease in activity, its increase was again observed (Fig. 2).

In the early stages after undergoing COVID-19, patients with AS often have a hypercoagulable syndrome. If available, it was recommended to take rivoroxaban at a dosage of 5-20 mg/day for 1-3 months. Also, such patients often have a low level of vitamin D 3, which in turn contributes to the progression of systemic osteoporosis. In such cases, it was recommended to take cholecalciferol at a dosage of 1000-5000 IU for 1-3 months.

Based on our studies, as well as taking into account foreign recommendations for the management of these patients, we have developed an algorithm for the secondary prevention of AS for patients who have had a coronavirus infection (Fig. 3.).

For the diagnosis of AS, early diagnosis of inflammatory back pain, the study of CLA, CRP, ASLO, RF of blood, the determination of the carriage of the HLA-B27 antigen, x-ray studies of the pelvic bones and spine, the detection of lesions of peripheral joints, the diagnosis of uveitis and enthesitis are recommended. When confirming the diagnosis, it is necessary to detect IgM antibodies, IgG COVID-19 antibodies, determine fibrogen, vitamin D3, study pro-inflammatory cytokines IL-6, IL-17, TNF-α.

Treatment of patients with AS begins with daily physical therapy, the selection of a basic anti-inflammatory drug (sulfasalazine, methotrexate, leflunamide or plaquenil), with inpatient treatment, parenteral corticosteroids, NSAIDs, intra-articular injections of corticosteroids, genetically engineered biological drugs (GEBP). In case of late visit of the patient to the doctor and the presence of ankylosis of the hip joints, surgical correction is recommended. With AS, long-term follow-up at the place of residence of a family doctor and / or a rheumatologist is necessary.

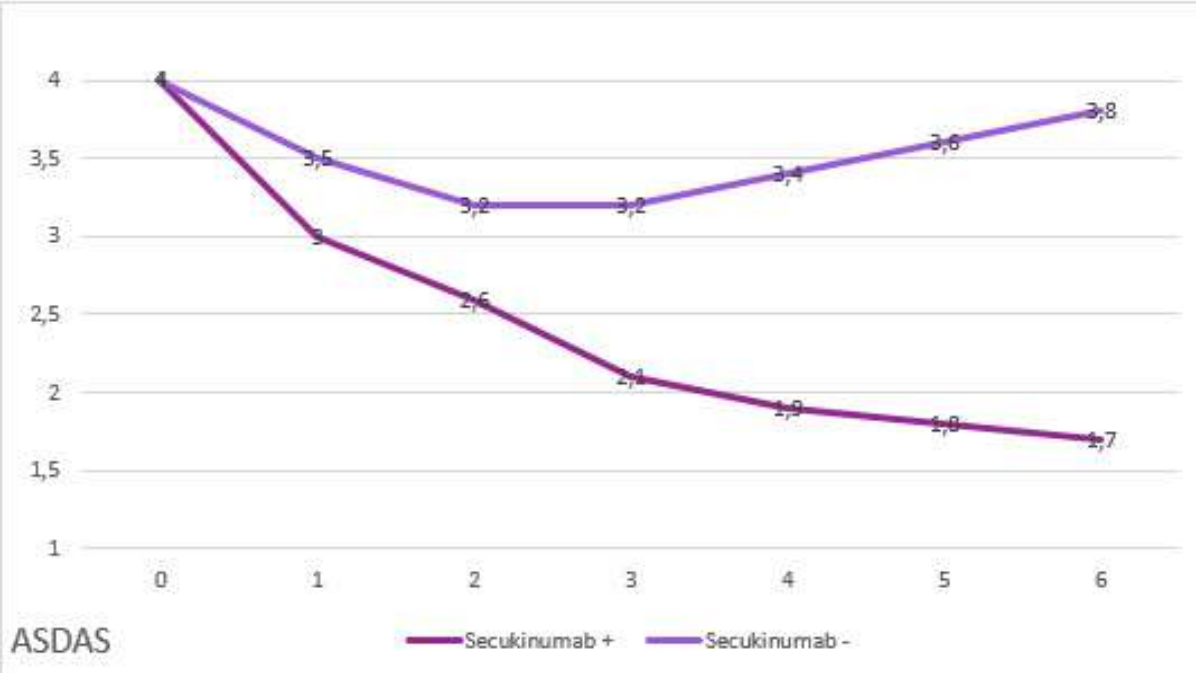

Fig. 2. Dynamics of AS activity according to ASDAS in patients treated with secukinumab and in the group receiving basic therapy.

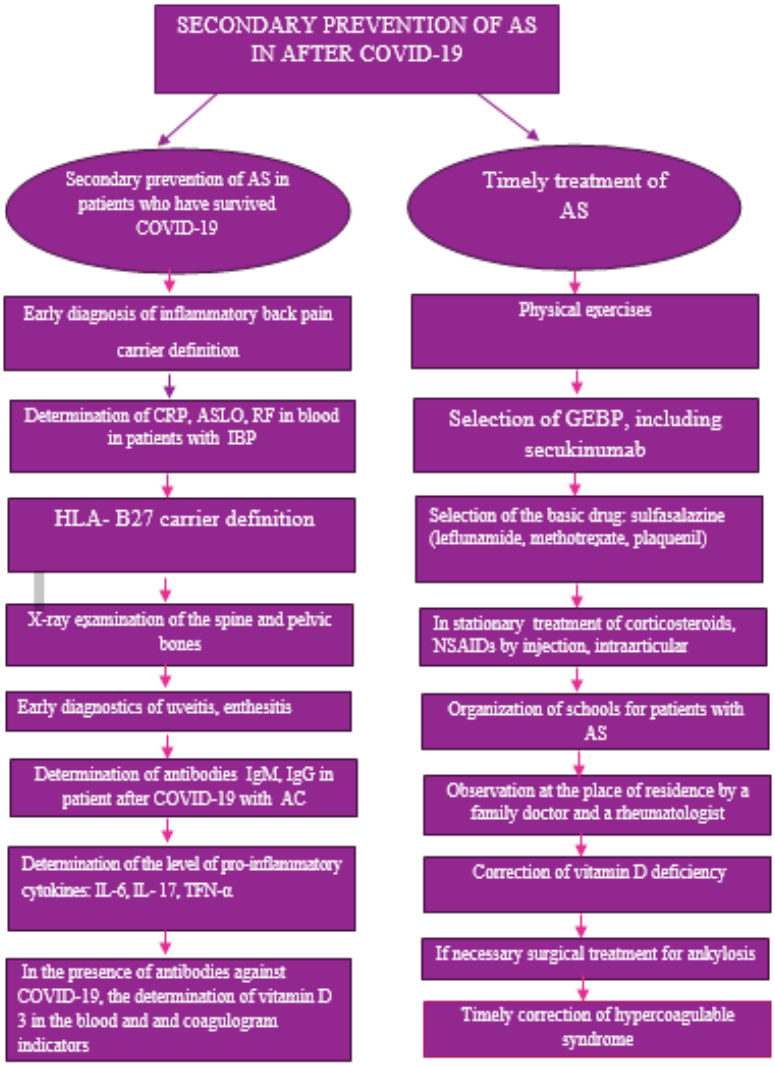

Fig.3. Algorithm for secondary prevention of AS in patients with COVID-19.

In patients with AS who have undergone COVID-19, given the persistence of the activity of the inflammatory process, it is recommended to use the IL-17 blocker secukinumab. Considering that hypercoagulable cider persists for a long time after COVID-19, if it is present, it is recommended to take rivoroxaban at a dosage of 5-20 mg for 1-3 months. To correct the lack of species on D3, it is recommended to take it at a dosage of 1000-5000 IU for 1-3 months.

Discussion:

According to the WHO definition, medical prevention is a type of activity of the health protection service, consisting of a set of measures aimed at early detection and reduction of the risk of developing pathologies, timely treatment and rehabilitation, as well as preventing complications of diseases. Prevention is divided into primary, secondary and tertiary [25]. Primary prevention is carried out to healthy individuals and consists of a set of measures aimed at maintaining a healthy lifestyle, as well as identifying people with risk factors for developing various diseases. Tertiary prevention is aimed at preventing complications of diseases, as well as rehabilitation of patients [4, 23].

Secondary prevention begins when the first symptoms of the disease appear. Secondary prevention also consists of two parts: early diagnosis and early treatment [25]. Early diagnosis of AS is very difficult in the early stages of the disease and in many cases the diagnosis is delayed by 5-7 years [5, 13]. An early symptom of AS is back pain and at this stage, patients rarely see a rheumatologist. Most patients have been treated by neurologists, neurosurgeons, traumatologists for many years with diagnoses of osteochondrosis, disc herniation, and the effectiveness of this treatment is very low [2]. Early detection of AS requires identification of inflammatory back pain (IBP) [2, 13]. The ASAS (2009) expert criteria should be used to diagnose IBP. According to these criteria, back pain is considered inflammatory if a patient with chronic pain (pain lasting more than 3 months) has 4 out of 5 of the following: 1) onset before the age of 40 years; 2) lasts more than 3 months; 3) gradual onset; 3) the pain does not go away at rest; 4) observation of pain at night and relief after getting up; 5) Loss and relief of pain after exercise [26]. If such symptoms are detected, the patient must examine the general blood analysis, rheumatic tests, immunological studies, HLA-B27, radiography or MRI / MSCT of the spine and pelvic bones to confirm the diagnosis [1, 2, 21]. One of the most common extraskeletal manifestations in patients with AS is uveitis [15]. Consultation with an ophthalmologist is recommended to detect uveitis. In recent years, autoantibodies to the CD 74 antigen (Anti-CD74) have been widely discussed; currently, it is considered as a candidate biomarker for diagnosing AS in the early stages of the disease [21]. The diagnosis of AS is made according to the modified New York criteria (1984) based on the presence of: IBP, limitation of movements in the spine, decreased chest excursion, the presence of sacroiliitis on X-ray [12]. The presence of uveitis, carriage of HLA-B27, enthesitis and morning stiffness for more than 30 minutes, damage to the peripheral joints are additional criteria for AS. After early detection of AS, it is necessary to detect the presence of IgM, IgG COVID-19 antibodies [6, 26]. In the presence of a high titer of antibodies and the absence of vaccination against COVID-19 from the anamnesis, it is recommended to conduct additional studies on: vitamin D in the blood, coagulogram, pro-inflammatory cytokines IL-6, IL-17, TNF-α [22].

AS is a chronic autoimmune disease, the goal of treatment of which is to achieve remission or low disease activity, which ensures the stabilization of the patient's functional capabilities, maintaining the quality of life and working capacity [5, 21, 26]. The modern strategy for the treatment of AS is based on the principles of "Treat to target" and implies the active prescription of drugs from the moment of diagnosis, frequent and objective monitoring of the patient's condition, changing the treatment regimen in the absence of a sufficient response to therapy up to achievement of treatment goals, after which constant dynamic monitoring. Drugs that are actively used in AS include: non-steroidal anti-inflammatory drugs; glucocorticoids; synthetic basic anti-inflammatory drugs (c-DMARDs); inhibitors of tumor necrosis factor α (ITNF-*α); interleukin 17 inhibitors (I*IL17) [15, 18, 21].

In our sample, after undergoing COVID-19, patients with AS showed a persistent increase in disease activity, with low efficiency from synthetic basic anti-inflammatory drugs. Given this fact, it is recommended to start basic treatment in combination with the IL-17 inhibitor secukinumab in patients with AS who have undergone COVID-19.

Thus, the use of this algorithm allows early diagnosis and timely treatment of AS in patients who have undergone COVID-19.

Conclusions:

1. The proposed algorithm for secondary prevention of AS in patients who have undergone COVID-19 allows rheumatologists, therapists, and family doctors to carry out the necessary tactics for early diagnosis and treatment of this disease.

2. Application of the AS secondary prevention algorithm will help prevent the progression of the disease, the development of complications and early disability in these patients.

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METHODS OF SECONDARY PREVENTION IN PATIENTS WITH ANKYLOSING SPONDYLOARTHRITIS UNDER COVID-19

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The article presents the results of our own studies of patients with ankylosing spondylitis (AS) who underwent COVID-19. Based on the conducted studies, methods of secondary prevention have been developed, including early diagnosis, as well as methods for the treatment of AS, taking into account the peculiarities of the course of COVID-19 and its impact on this disease.

Keywords: *COVID-19, ankylosing spondylitis, secondary prevention.*