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The Effect of Nonsteroidal Anti-Inflammatory Drugs on the Progression of Sacroiliitis in Patients With Axial Spondyloarthritis

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Abstract: The aim of the study was to compare the effect of constant intake of nonsteroidal anti–inflammatory drugs (NSAIDs) and their on-demand administration on the activity and radiological progression of early axial spondyloarthritis (accSpA).

Material and methods. The study included patients from the CORSAIR cohort who met the criteria of the ASAS 2009 ACSPA. The present analysis included 68 patients who were followed up for at least 24 months. The age at the time of inclusion in the study was 28.5±5.8 years, the average duration of the disease was 24.1±15.4 months, 63 (92.6%) patients were positive for HLA–B27. Patients were divided into two groups: in the first (n=35), patients received NSAIDs continuously during the follow–up period at maximum therapeutic doses, in the second (n=33), NSAIDs were prescribed "on demand" depending on the presence and severity of back pain.

Results and discussion. In the first group, after 2 years of follow-up, the median stage of radiological the sacroiliitis score (SI) has not changed and remains equal to 4 points, in the second group this indicator is for the observed period significantly increased from 3 to 4 points ($p<0.05$). Initially, the patient groups did not differ in the level of C-reactive protein (CRP), ASDAS-CRP and BASFI indices, but the BASDAI index was higher in the first group ($p<0.05$). The number of patients with active SI according to magnetic resonance imaging (MRI) and the degree of its severity did not significantly differ in both groups. After 2 years, all patients retained low disease activity according to ASDAS-CRP, BASDAI and CRP levels, as well as data the indicators did not differ significantly in both groups, the BASFI index became higher in the first group. The number of patients with active SI decreased according to MRI data, but there were no differences between the groups.

Conclusion. In patients with early accSpA, the constant use of NSAIDs allows to slow down the X-ray progression to a greater extent than the "on-demand" intake.

Key words: spondyloarthritis; axial spondyloarthritis; ankylosing spondylitis; non-pathogenic axial spondyloarthritis; sacroiliitis; radiological progression.

INTRODUCTION

Currently, there are two points of view on the evolution of AXSP. According to the first hp, ACSPA is the initial stage of AS, which is confirmed by the similarity of their clinical manifestations and the gradual development of bone injuries corresponding to reliable radiological SI (rSI), as a result of which a typical picture of AS is formed after some time. In 50-70% of patients with hp-ACSPA, by the 5th year of the disease, rSI develops, i.e., reliable AS. According to the second point of view, hp-axSpA is a separate nosological unit from AS. Currently, the theory has more supporters, according to which a certain sequence of pathological processes in the sacroiliac joints (CPS) is assumed to determine the evolution of axSpA. Initially, inflammation occurs in the bone CPS tissue detected by MRI (active SI/spondylitis), which, in turn, leads to erosion of bone tissue. After the active inflammation subsides, osteosclerosis forms at the site of bone damage and subsequently new bone tissue characterized by hyperproliferation with gradual ankylosing of the CPS and/or the growth of syndesmophytes/enthesophytes. The X-ray progression in patients with axSpA has not been studied sufficiently, especially at an early stage of the disease development. Based on the results of a 12-year

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follow-up of a Dutch cohort of patients with AS (OASIS) revealed that the predictor of faster bone proliferation in the spine in patients with reliable AS is the high activity of the disease according to the ASDAS-CRP index. An analysis of data from a two-year follow-up of a German cohort of patients with early accSpA (GESPIC) showed a direct relationship between high values of acute phase parameters inflammation (ESR and CRP levels) and cigarette smoking with progressive spinal injury. Later, the same authors published data from a study that revealed a positive correlation between the ASDAS-CRP index and the formation of syndesmophytes. However, these studies took into account all patients with acsSpA, including both AS and hp-acsSpA, and progression was determined by the growth of syndesmophytes, while the issues of disease progression at an early stage were not studied. It should be noted that the process of syndesmophyte growth in patients with reliable AS, it is natural and proceeds faster if there is already at least one syndesmophyte, whereas they are absent in the early stages of the disease. Since the evolution of ACSSP has been poorly studied, more and more attention has been paid to this issue recently. Several studies have compared the clinical manifestations of AS and hp-axSpA. It has been shown that they are comparable with each other in terms of disease activity, pain severity and impact on quality of life. At the same time, there are more men among patients with AS, unlike hp-axSpA, which occurs with the same frequency in men and women. Also, in patients with AS, more radiological changes in the spine are detected, and the functional status is worse, this is partly due to the presence of syndesmophytes and a higher level of C-reactive protein (CRP), than with hp-axSpA. However, despite these differences, treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and tumor necrosis factor α (iFNOa) inhibitors is effective for both groups. Therefore, we have previously suggested that hp-expa is an early stage of AS.The aim of the study was to compare the effect of constant NSAID intake and the use of these drugs "on demand" on the activity and X–ray progression of early ACSP.

MATERIALS AND METHODS OF RESEARCH

Methods used in research work: assessment of the clinical activity of acsSpA and the functional status of patients was performed according to generally accepted recommendations using ASAS indices. BASDAI and ASDAS-CRP indices were used to determine the activity of the disease. The functional status was assessed according to the BASFI index. The MASES index was used to calculate painful entheses. In addition to clinical examination and standard laboratory tests (general blood test, biochemical blood test, research The presence of HLAB27 was determined in all patients, and pelvic bone radiography and MRI of the CPS were performed. Active inflammatory changes (VI) were determined in the fat suppression mode (STIR) with a slice thickness of 4 mm. The detection of obvious subchondral edema of the bone marrow (osteitis), visualized as a hyperintensive signal in the STIR mode, was regarded as an MRI sign of SI. The presence of VI in the CPS and spine was noted if signs of osteitis were detected on at least two sections or if more than two hyperintensive foci of active inflammation on one slice. The British LEEDS account was used to calculate the severity of active SI. Patients were comprehensively evaluated at the beginning of the study and after 2 years. To assess the progression of the disease, the sum of the radiological stages of SI in the left and right CPS was determined. The diagnosis of AS was established according to the modified New York criteria. The 2009 ASAS criteria were used to diagnose hp-ACSPA. for spondyloarthritis with predominant axial symptoms. Statistical data processing was carried out using an application software package Statistica 10.0 (StatSoft, USA). The analysis included generally accepted descriptive statistics procedures and nonparametric comparison methods. Each patient signed an informed consent to participate in the study. The study was approved by the local ethics committee. The present analysis included 68 patients who were followed up for at least 24 months. The average age was 28.5±5.8 years, the average duration of the disease was 24.1±15.4 months; 63 (92.6%) patients were positive for HLA-B27. The patients were divided into two groups: in the first (n=35) continuous NSAID treatment was carried out during the follow–up period at maximum therapeutic doses, in the second (n=33) NSAIDs were prescribed "on demand" depending on the presence and severity of back pain. The maximum therapeutic dose was calculated according to the NSAID index. Since the effectiveness of various NSAIDs in acsSpA does not differ significantly, no preference was given to any drugs in this study. Monitoring of the safety of long-term use of NSAIDs in acsSpA was carried out according to the

recommendations of the Russian Expert Group on the study of SpA. With continued high clinical and laboratory activity of the disease after consistent administration αFNOa therapy was initiated in patients with two NSAIDs for 1 month according to the recommendations. Initially, αFNOa was received by three patients (4.4%), after 2 years of follow-up, their number increased to 14 (20.5%).

THE RESULTS AND THEIR DISCUSSION

Initially, AS was detected in 24 of 35 (68.5%) patients of the first group and in 16 of 33 (48.4%) patients of the second group ($p>0.05$), hp-ACSPA – respectively in 11 (31.5%) and 17 (51.6%; $p>0.05$; Table 1). When including the group of patients who took NSAIDs constantly and "on demand", they did not differ in ASDAS-CRP, however, the BASDAI index it was higher in the first group ($p<0.05$). The groups also did not differ in terms of the CRP level and the BASFI index. The number of patients with active SI according to MRI data and the degree of its severity did not significantly differ in both groups. 2 years after the start of follow–up, the number of patients with AS in the first group was 29 (82.8%), in the second – 22 (66.6%; $p>0.05$;). Thus, in the first group there were 5 (14.2%), and in the second - 6 (18.1%) patients from the group hp-axSpA moved to the AS group, i.e. they developed a reliable SI, confirmed by radiography. After 2 years, all patients retained low disease activity according to ASDAS-CRP and BASDAI, the level of CRP; Also, these indicators did not significantly differ in both groups, whereas the BASFI index in the first group became higher than in the second. The number of patients with MRI signs of active SI decreased in both groups, and there were no differences in this indicator between the groups. The NSAID index was significantly lower in the second group. In the group of continuous NSAID intake after 2 years of follow-up, the median of the stage of rSI did not change and remained equal to 4.0 points, in the group of NSAID intake "on demand" this indicator significantly increased from 3.0 to 4.0 points ($p<0.05$), respectively. NSAIDs are first-line drugs for both AS and hp-ACSPA. According to the recommendations of ASAS, and domestic SpA experts, for patients with AS, continuous use should be considered preferable, since it can provide not only a decrease in disease activity, but also a slowdown in the progression of structural changes by suppressing pathological proliferation of bone tissue in the axial skeleton. However, it is still not clear which reception mode NSAIDs are preferred in patients with early ACCSA. Data on the effect of NSAIDs on X-ray progression is very controversial, since previous studies conducted on a German cohort of patients with early axSpA relied on the presence of syndesmophytes, according to the MSASS index in patients with both hp-expa and reliable AS. It is known that the process of osteoproliferation in patients with acsSpA begins with CPS. In the present study, when comparing constant intake NSAIDs with an on-demand regimen, we revealed a significantly greater radiological progression of SI in the second case. A decrease in bone proliferation may be associated with inhibition of COX2-mediated prostaglandin synthesis, which was confirmed in experimental models in mice. Tibial fracture in mice with suppressed activity COX2 took longer to heal than when COX1 was suppressed or when both COX isoenzymes were active.

CONCLUSIONS

However, despite the greater radiological progression in the on-demand NSAID group, the BASFI index was worse after 1 and 2 years in the continuous intake group, which may be due to the initially large number of patients with significant AS in this group. Disease activity according to the main indices, including the level of CRP. It remained low after 2 years of follow-up, possibly due to the rapid achievement of low disease activity/remission in the early stages of the disease. Thus, in patients with early ACCSA, the constant use of NSAIDs can slow down the radiological progression of SI to a greater extent than the use of these drugs "on demand".

LITERATURE

1. Хамраева, Н. А., Султонов, И. И., & Хасанов, Ф. Ш. У. (2019). Кожные проявления у больных системной красной волчанкой. Вопросы науки и образования, (28 (77)), 128-131.
2. Sultonov, I. I., Kh, Z. S., Ruzybakieva, M. R., Kireev, V. V., Aripova, T. U., & Suyarov, A. A. (2021). Pharmacogenetic Aspects of Drug Resistance in Rheumatoid Arthritis. Annals of the Romanian Society for Cell Biology, 4147-4150.

3. Тоиров, А. Э., Султонов, И. И., & Тоиров, Э. С. (2020). ЗНАЧЕНИЕ ДИСФУНКЦИИ ПОЧЕК У БОЛЬНЫХ ОСТРЫМ ИНФАРКТОМ МИОКАРДА НА ФОНЕ САХАРНОГО ДИАБЕТА 2-ГО ТИПА. Вестник науки и образования, (9-3 (87)), 86-91.
4. Kireev, V. V., & Sultonov, I. I. (2021). Genetic Engineered Preparations-An Innovative Approach in the Treatment of Rheumatoid Arthritis. Annals of the Romanian Society for Cell Biology, 4114-4119.
5. Hamraeva, N. A., Sultonov, I. I., & Hasanov, F. S. (2020). Systemic lupus erythematosus treatment strategy. Journal of Critical Reviews, 7(9), 269-270.
6. Иргашева, У. З., Султонов, И. И., & Тоиров, Д. Р. (2013). Признаки дебюта системной красной волчанки. Академический журнал Западной Сибири, 9(1), 15-15.
7. Xasanov, F. S., & Sultonov, I. I. (2023). RHEUMATOID ARTHRITIS TREATED WITH DMARDS AND CARDIOVASCULAR DISEASE RISK. Oriental Journal of Medicine and Pharmacology, 3(02), 45-52.
8. Sultonov, I. I., Xasanov, F. S., Eshmuratov, S., Uralov, R. S., Shukurova, D., & Ziyadullayev, S. X. Predictors of Systemic Lupus Erythematosus: A Case-control Study. International journal of health sciences, 6(S10), 175-182.
9. Ziyadullaev, S. K., Sultonov, I. I., Dushanova, G. A., & Akbarovna, K. S. (2021). The Effectiveness of Pharmacotherapy for Dmards with Ra Depending On the C3435t Polymorphism of the Mdr1 Gene. Int. J. of Aquatic Science, 12(3), 2908-2916.
10. Ibragimov, K., Sultonov, I., & Ravshanova, M. (2024). The Effectiveness of the Combination Therapy with biologic DMARDS in Rheumatoid Arthritis. Frontiers of Global Science, 2(1), 17-24.
11. Islomovich, S. I., Alisherovna, K. M., & Djamshedovna, K. D. (2024). FACTORS OF OSTEOPOROSIS IN PATIENTS WITH CORONARY HEART DISEASE IN COMBINATION WITH RHEUMATOID ARTHRITIS. Ta'lim innovatsiyasi va integratsiyasi, 31(2), 132-138.
12. Sobirov, A., & Sultonov, I. (2024). COMPREHENSIVE ANALYSIS OF CLINICAL NEUROPSYCHOLOGICAL AND NEUROIMAGING ASPECTS OF ALZHEIMER'S DISEASE. Frontiers of Global Science, 2(1).
13. Ilkhom, S. (2023). CAJAM–VOLUME 1. ISSUE 1. 2023. Central Asian Journal of Advanced Medicine, 1(01), 16-19.
14. Islomovich, S. I. (2024). FEATURES OF THE COURSE OF PREGNANCY IN RHEUMATOID ARTHRITIS. International journal of medical sciences, 4(10), 77-84.
15. Islomovich, S. I. (2024). GENDER CHARACTERISTICS OF THE CURRENT RHEUMATOID ARTHRITIS. International journal of medical sciences, 4(10), 3-8.
16. Djamshedovna, K. D., Alisherovna, K. M., & Islomovich, S. I. (2024). ARTERIAL HYPERTENSION IN RHEUMATOID ARTHRITIS. Ta'lim innovatsiyasi va integratsiyasi, 31(2), 139-145.
17. Nizamitdinovich, K. S., Alisherovna, K. M., & Islomovich, S. I. (2024). CLINICAL COURSE OF BRONCHIAL ASTHMA IN PATIENTS WITH THYROID DISEASES. Ta'lim innovatsiyasi va integratsiyasi, 31(2), 181-187.
18. Alisherovna, K. M., Nizamitdinovich, K. S., & Islomovich, S. I. (2024). THERAPY OF RHEUMATOID ARTHRITIS DURING PREGNANCYTHE. Ta'lim innovatsiyasi va integratsiyasi, 31(2), 172-180.
19. Alisherovna, K. M., Islomovich, S. I., & Djamshedovna, K. D. (2024). PSYCHOEMOTIONAL STATE AND QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS. Ta'lim innovatsiyasi va integratsiyasi, 31(2), 124-131.

20. Alisherovna, K. M., Nizamitdinovich, K. S., & Islomovich, S. I. (2024). FEATURES OF BONE MINERAL DENSITY IN PATIENTS WITH DISEASES OF THE DIGESTIVE SYSTEM. Ta'lim innovatsiyasi va integratsiyasi, 31(2), 162-171.
21. Sherbekovich, U. R. (2024). DISORDERS OF THE DIASTOLIC FUNCTION OF THE LEFT VENTRICLE WITH CORONARY HEART DISEASE. International journal of medical sciences, 4(11), 49-53.
22. Sherbekovich, U. R., & Eldorovich, E. S. (2024). PROFILE OF AUTOANTIBODIES IN SYSTEMIC SCLERODERMA. International journal of medical sciences, 4(05), 257-265.
23. Eldorovich, E. S., & Sherbekovich, U. R. (2024). THE CLINICAL SIGNIFICANCE OF INTERLEUKIN-4 IN SYSTEMIC SCLERODERMA. Spectrum Journal of Innovation, Reforms and Development, 27, 51-58.
24. Sherbekovich, U. R., & Eldorovich, E. S. (2024). SEVERITY INDEX IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS. Spectrum Journal of Innovation, Reforms and Development, 27, 75-82.
25. Eldorovich, E. S., & Sherbekovich, U. R. (2024). DYNAMIC CHANGES IN THE ACTIVITY INDEX AND THE TOTAL SEVERITY INDEX IN PATIENTS WITH SYSTEMIC SCLERODERMA AND INTERSTITIAL LUNG DISEASE OVER A 5-YEAR FOLLOW-UP PERIOD. International journal of medical sciences, 4(05), 281-289.
26. Sherbek o'g'li, U. R. JIGAR TRANSPLANTATSIYASI O'TKAZILGAN BEMORLARDA GEPATOSELLULYAR KARSINOMA RIVOJLANISHIDA KALSINEVRIN INGBITORLARINI (CYA-SIKLOSPORIN A VA TAC-TAKROLIMUS) ORNI.
27. Абдушукурова, К. Р., Исламова, К. А., Хамраева, Н. А., & Уралов, Р. Ш. (2023). ФФЕКТИВНОСТЬ ЛЕЧЕНИЯ РЕВМАТОИДНОГО АРТРИТА. IQRO, 2(2), 194-200.
28. Тоиров, Э., Исломова, К., & Уралов, Р. (2019). Эффективность комплексного лечения раннего остеоартроза. Журнал вестник врача, 1(3), 99-103.
29. Исламова, К. А., Абдушукурова, К. Р., Хамраева, Н. А., & Эшмуратов, С. Э. (2023). ЭФФЕКТИВНОСТЬ ВНУТРИСУСТАВНОГО ВВЕДЕНИЯ ГИАЛУРОМ ХОНДРО ПРИ РАННЕМ ОСТЕОАРТРОЗЕ. IQRO, 2(2), 186-193.
30. Khusainova, M. A., Eshmamatova, F. B., Ismoilova, K. T., & Mamadiyorova, M. M. (2023). METABOLIC SYNDROME IN RHEUMATOID ARTHRITIS AS A CRITERION OF CARDIOVASCULAR RISK. Oriental renaissance: Innovative, educational, natural and social sciences, 3(1), 331-339.
31. Khabibovna, Y. S., Alisherovna, K. M., Totlibayevich, Y. S., & Davranovna, M. K. (2023). PAINLESS CARDIAC ISCHEMIA AND RHEUMATOID ARTHRIT. Journal of new century innovations, 29(1), 98-105.
32. Davranovna, M. K. D. K., Alisherovna, K. M., & Erkinovna, K. Z. (2024). CARDIAC ARRHYTHMIAS IN PATIENTS WITH RHEUMATOID ARTHRITIS. Spectrum Journal of Innovation, Reforms and Development, 26, 65-71.
33. Khusainova, M. A., Khaydarov, S. N., Makhmudova, K. D., & Nayimov, A. S. (2023). Prevalence of bronchiolitis in patients with Rheumatoid arthritis. Science and Education, 4(5), 232-241.
34. Khusainova, M. A., Vakhidov, J. J., Khayitov, S. M., & Mamadiyorova, M. M. (2023). Cardiac arrhythmias in patients with rheumatoid arthritis. Science and Education, 4(2), 130-137.
35. Alisherovna, K. M., Erkinovna, K. Z., Djamshedovna, K. D., & Nizamitdinovich, K. S. (2023). QUALITY OF LIFE PATIENTS WITH OSTEOARTHRITIS. Journal of new century innovations, 36(1), 164-175.

36. Alisherovna, K. M., & Erkinovna, K. Z. (2022). Assessment of the Immune-Inflammatory Relationship in Patients with Chronic Heart Failure with Rheumatoid Arthritis. Central Asian Journal of Medical and Natural Science, 3(2), 373-377.

37. Alisherovna, K. M., Baxtiyorovich, Z. M., & Anvarovich, N. J. (2022). To Assess The Condition Of The Myocardium In Patients Chronic Heart Failure On The Background Of Rheumatoid Arthritis. Spectrum Journal of Innovation, Reforms and Development, 4, 210-215.

38. Alisherovna, K. M., Akramovna, I. K., & Kairatovna, R. A. (2024). THE EFFECTIVENESS OF TREATMENT OF PATIENTS WITH OSTEOARTHRITIS WITH CARDIOVASCULAR DISORDERS IN METABOLIC SYNDROME. Ta'lim innovatsiyasi va integratsiyasi, 18(5), 223-230.

39. Erkinovna, K. Z., Alisherovna, K. M., Bakhtiyorovich, U. J., & Djamshedovna, K. D. (2023). METABOLIC SYNDROME IN RHEUMATOID ARTHRITIS. Journal of new century innovations, 38(2), 203-211.

40. Khusainova, M. A., Khaydarov, S. N., Uzokov, J. B., & Shonazarova, N. K. (2023). QUALITY OF LIFE IN PATIENTS WITH CHOLELITHIASIS IN THE LONG-TERM PERIOD AFTER CHOLECYSTECTOMY. Oriental renaissance: Innovative, educational, natural and social sciences, 3(2), 231-239.