
Evaluation of the Effectiveness of Meloxicam in the Treatment of Patients with Rheumatoid Arthritis in Older Age Groups

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Abstract: The article presents the results of a study of the clinical efficacy and tolerability of a new generation of non-steroidal anti-inflammatory drugs (NSAIDs) meloxicam 10 mg cyclooxygenase inhibitors (COX-2 inhibitor) in the treatment of rheumatoid arthritis in patients of older age groups. In 35 patients with rheumatoid arthritis (RA) of both sexes aged 45-65 years, an open clinical study of the action of meloxicam was performed. During the treatment period, basic therapy, drugs that improve heart function, diuretics and antiplatelet agents were prescribed. Controlled clinical and laboratory parameters were assessed before the inclusion of patients in the study and after the end of therapy.

Keywords: rheumatoid arthritis, NSAIDs, cyclooxygenase (COX-2) inhibitors.

Introduction. Rheumatoid arthritis occurs in 1-3% of the world's population (Gabriel 2016). A significant prevalence of RA, mainly among the working age group of the population, leads to chronicity of the disease and a progressive course, a high frequency of loss of professional ability to work in patients [1, 2]. The increase in the number of elderly and senile people observed in Uzbekistan, as in many other countries, is accompanied by an increase in the number of diseases associated with the aging process - osteoarthritis, rheumatoid arthritis, osteoporosis, diabetes mellitus, obesity, Alzheimer's disease [3, 4]. The process of human aging is accompanied by changes in the genetic apparatus of the cell, the development of a number of diseases. Due to the fact that physiological aging is realized in accordance with the genetic program, all people have uniform signs of aging and old age, 85% die from the same diseases: atherosclerosis, diabetes mellitus, immune suppression, cancer, rheumatoid arthritis and other autoimmune diseases [3, 4]. The main development of diseases such as rheumatoid arthritis, osteoarthritis, spondylarthrosis, osteochondrosis, and osteoporosis is the involution of connective tissue [5]. With aging, its cellular composition changes, the ratio of the main structural macromolecules of the intercellular substance. The content of collagen and the amount of connective tissue in various organs increases, the content of structural glycoproteins, glycosaminoglycans, proteoglycans, and the amount of elastic fibers decrease. With the development of disorders in the connective tissue, not only age-related changes in the organs of the musculoskeletal system, but also in blood vessels are associated [5,6]. The transformation of connective tissue with aging is accompanied by a violation of the structure of articular and intervertebral cartilage, bone mineralization, skeletal strength, and the occurrence of deformities. Involutional changes in the body increase from the age of 35 to 50-55 years for women, 55-60 years for men [7]. Rheumatoid arthritis is the most common form of articular pathology, one of the main causes of chronic pain, before temporary disability and disability. In the prevention of rheumatological diseases, in addition to rheumatoid arthritis in the elderly, it allows normalizing the processes of bone remodeling, improving its strength characteristics, reducing the risk of fractures, and improving the quality of life [8, 9]. Wide sections of the population need prevention, and above all,

rheumatological diseases will remain in a state of prolonged stress, alcohol abusers, during radiation therapy, and others.

It should be canceled that without an in-depth study of the issues of etiology, pathogenesis, diagnosis, prevention and treatment of rheumatoid arthritis in the elderly, without explanatory work among the population, training of medical staff, the fight against the epidemic of these diseases will be ineffective. The development of an effective prevention strategy on a large scale is also required. The leading clinical manifestation of RA is articular syndrome of varying severity [3,4]. The development of arthritis from several weeks to several months may be preceded by increased fatigue, decreased appetite, weight loss, arthralgia, subfebrile temperature, increased sweating, moderate anemia, increased erythrocyte sedimentation rate (ESR), and lymphadenopathy [10]. Options for the onset (debut) of RA can be varied: symmetrical polyarthritis with a gradual increase in pain and stiffness, mainly in the small joints of the hands; acute polyarthritis with predominant involvement of the joints of the hands and feet, severe morning stiffness, mono- or oligoarthritis of the knee or shoulder joints, followed by rapid involvement of the small joints of the hands and feet acute monoarthritis of large joints; acute oligo- or polyarthritis with systemic manifestations (fever, lymphadenopathy, hepatosplenomegaly); recurrent bursitis and tenosynovitis of the wrist joints; acute polyarthritis in the elderly with multiple lesions of small and large joints, severe pain, diffuse edema and limited joint mobility; generalized myalgia, stiffness, bilateral carpal tunnel syndrome, weight loss. Usually seen in elderly patients. Signs characteristic of RA appear later. According to the nature of the course and progression of joint destruction and extra-articular manifestations, several variants of the course of RA are distinguished: a rapidly progressive course: high disease activity, rapid development of joint destruction, severe extra-articular lesions; progressive course: joint destruction increases, new joints are involved, extra-articular lesions develop; intermittent course: periodically there is a complete or partial remission (spontaneous or induced by treatment), followed by an exacerbation with the involvement of previously unaffected joints in the process; prolonged spontaneous clinical remission. The involvement of the joints in the pathological process is the leading one in the clinical picture of RA. In the initial period, 1/3 of the patients had arthralgia, aggravated by movement, 2/3 had symmetrical arthritis of the small joints of the hands and feet. A characteristic sign of synovial inflammation is morning stiffness in the joints, its duration usually correlates with the intensity of inflammation and is at least 1 hour. Pain and stiffness are most intense in the morning and gradually subside in the evening. As a rule, the second or third metacarpophalangeal, proximal interphalangeal and wrist joints are involved first, as a rule, in RA, less often metatarsophalangeal joints. Then the frequency of the lesion is followed by the knee, elbow, and ankle joints. A number of joints in the debut of RA remain intact (“exclusion joints”) — distal interphalangeal, first metacarpophalangeal joint of the thumb, proximal interphalangeal joint of the little finger. Joint damage in RA has its own clinical features. Involvement of the joints of the hands is most typical for RA (Fig. 2). The metacarpophalangeal and proximal interphalangeal joints are the first to be affected. Initially, there is pain and swelling of the joint associated with inflammation and thickening of the synovial membrane and soft tissues of the joint, the accumulation of excess synovial fluid. Movement is limited due to pain. The patient holds the joint in flexion in order to reduce the tension of the joint capsule [1,5,8]. A patient with an established diagnosis of rheumatoid arthritis should be prescribed a drug from the DMARD group, which, with a good clinical effect, can be used as the only method of therapy [9]. Other remedies are used as needed. The patient should be informed about the nature of his disease, the course, prognosis, the need for long-term complex treatment, as well as possible adverse reactions and treatment control scheme, adverse combinations with other drugs (in particular, alcohol), possible activation of foci of chronic infection during treatment, the expediency of temporary cancellation of

immunosuppressive drugs in the event of acute infectious diseases, the need for contraception during treatment [2,8,9]. Therapy for rheumatoid arthritis should be prescribed by a rheumatologist and carried out under his supervision. Treatment with biological preparations can only be carried out under the supervision of a rheumatologist who has sufficient knowledge and experience to carry it out. Therapy is long-term and involves periodic monitoring of disease activity and evaluation of response to therapy. A simplified algorithm is presented in the Monitoring of disease activity and response to therapy includes an assessment of articular status indicators (number of painful and swollen joints, etc.), acute phase blood parameters (ESR, CRP), assessment of pain and disease activity on a visual analogue scale, assessment of the patient's functional activity in daily activities using the Russian version of the Health Questionnaire (HAQ). There are methods recognized by the international community of rheumatologists to quantify response to treatment using the Disease Activity Score (DAS) recommended by the European League Against Rheumatism (EULAR) and the criteria of the American College of Rheumatology (ACR) [1]. In addition, the safety of the therapy administered to the patient should be monitored (in accordance with both the formulary and existing clinical guidelines). Due to the fact that the erosive process can develop even with low inflammatory activity, in addition to assessing the activity of the disease and the response to therapy, radiography of the joints is mandatory. The progression of destructive changes in the joints is assessed by standard radiography of the hands and feet using radiological classification of the stages of rheumatoid arthritis, quantitative methods according to the Sharp and Larsen indices. In order to monitor the patient's condition, the examination is recommended to be carried out at regular intervals [4,5]. The leading place in the treatment of diseases of the musculoskeletal system is occupied by NSAIDs, which have analgesic and anti-inflammatory effects, and also contribute to the inhibition of the pathological process [3,10].

Non-steroidal anti-inflammatory drugs are one of the most popular drugs in general therapeutic practice. The main indications for their use are pain of various localization, inflammation and fever of almost any etiology. Such a positive reaction of these drugs is mainly associated with the suppression of the is form of 1-cyclooxygenase (COX-1) and positive therapeutic effects with another is form of COX-2 [2, 10].

Objective. The aim of the study is to study the effect of the drug meloxicam, which is prescribed as a short course to patients with severe pain and disability in RA.

Materials and methods. The study included 35 patients of both sexes aged 45 to 63 years, whose average age was 52 years old, suffering from RA and requiring NSAIDs due to the activity of the disease or the severity of the pain syndrome. The duration of the disease varied from one to 30 years. Rheumatoid factor was found in 58% of the examined patients. Inflammatory activity of the 2nd degree was present in 64% of patients, minimal - in 22% and in the remaining 14% - 3rd degrees. During X-ray examination, stages II-III according to Stein broker were determined more often. Stage I was established in 6 patients, stage II - in 18, stage III in 8, stage IV in 3 patients. 51% of patients had II degree of functional insufficiency of the joints Significant concomitant pathology affecting the tolerability of NSAIDs was represented by the following diseases: lesions of the gastrointestinal mucosa, including gastritis, peptic ulcer of the stomach and duodenum 12 without exacerbation, which were diagnosed according to EGDS 31%, 18%, and 8% , respectively, cardiovascular pathology, represented by hypertension and coronary heart disease, was present in 28% and 8% of patients. Also, in isolated cases, patients had cholelithiasis and thyroid pathology. All patients received Meloxicam at a dose of 10 mg 1 time per day as intramuscular injections for 5 days, the condition of the patients was assessed 3 times: before treatment, 5 days later and 2 weeks after the end of treatment to assess the aftereffect. In addition to general clinical and

radiological studies, the intensity of pain syndrome was determined by VAS, the number of inflamed joints, the Ritchie index, the functional state of the joints (the ability of patients to get out of bed on their own, walk on a flat surface, go down and up stairs). All criteria were evaluated before and after treatment. Among all the studied patients, 7 patients received appropriate corrective therapy with antihypertensive drugs due to concomitant hypertension. Erosive-ulcerative lesions of the gastrointestinal tract in history had 12 patients, of which at the time of inclusion in the study gastroprotective drugs received 5 patients. The efficacy of loxidol in patients with RA was evaluated separately. At the time of inclusion in the study, basic drugs (methotrexate, sulfasalazine) were received by 15 people, glucocorticosteroids at a dose of not more than 10 mg / day per prednisone were given to 12 patients, in all patients, basic therapy and glucocorticosteroids remained unchanged for at least 4 weeks

Results. As a result of the therapy, all clinical manifestations of the articular syndrome underwent significant positive dynamics. The action of loxidol lasted an average of 5.1 ± 18 hours.

In the majority of 24 patients (61.6%) meloxicam was well tolerated, in 6 patients (17.2%) the tolerance was regarded as satisfactory, with no serious adverse reactions noted. In 3 patients (8.5%), side effects were noted (moderate gastralgia, slight nausea, headache), only 2 (5.8%) patients had insufficient efficacy of the drug. Efficiency indicators of articular syndrome during meloxicam therapy in patients with RA $n=35$

Parameters	Before treatment	One week after treatment
Number of painful joints	$8,3 \pm 4,6$	$5,5 \pm 4,0$
Number of inflamed joints	$5,1 \pm 3,1$	$3,0 \pm 2,5$
Ritchie index, points	$16,1 \pm 10,2$	$10,8 \pm 7,9$
VAS Pain on	$43,1 \pm 19,3$	$27,0 \pm 17,1$
Pain on movement,	$64,7 \pm 19,0$	$45,8 \pm 19,5$
Pain at rest, VAS palpation	$46,4 \pm 21,7$	$27,7 \pm 19,0$

$p < 0,005$ $p < 0,001$

As a result of the study, it was found that a short course of meloxicam at a dose of 15 mg 1 time per day in the form of intramuscular injections for 5 days significantly reduces the intensity of the pain syndrome, and a regression of the clinical symptoms of the disease was also noted. Findings. "Meloxicam" is effective when administered parenterally in a regimen of 5 injections daily to reduce the severity of pain in patients with RA disease. On the part of the drug, the frequency of side effects does not depend on the dose of the drug. Even a monthly course of application of loxidol significantly improves the quality of life of patients and, first of all, their role and physical functioning.

Literature

1. Бадритдинова М.Н., Тиллоева Ш.Ш. Диагностика и лечение ревматоидного артрита у пожилых. Монография// Бухара. – 2016. - 100 с.
2. Бадритдинова М.Н., Тиллоева Ш.Ш., Линас Шумскас. Rheumatoid Arthritis in the Elderly. Monograph// Bukhara. №8н-м/213 “Дурдона”. - 2019. – 96 с.
3. Насонов Е.Л. Современное учение о селективных ингибиторов ЦОГ-2. Новые аспекты применения целокса. Научн.прокт.ревматол.2003 №4
4. Tillaeva Sh. Sh., Badritdinova M.N., Soliev A.U., Akhmedova Sh.M. Currency and diagnostic criteria of rheumatoid arthritis in patients of senior age groups// Asian

Journal of Multidimensional Research. Reviewed International Journal (AJMR) -2018.- Vol.7, - P. 184-188.

5. Тиллаева Ш.Ш, Халилова Ф.А. Течение и диагностические критерии ревматоидного артрита у пациентов старших возрастных групп // Новый день в медицине. -2018. - №3 (23). - С. 70-72
6. Ярославцева Н.В. Липоксикам в неврологии. Неврол. психиатрии. 2006 г. №7 (122)
7. Перспективы применения современного противовоспалительного препарата Амелотекс (мелоксикам) в клинической практике. Елисеев М.С. Ремедиум. 2008 №11 стр.22-23
8. Aletaha D., Neogi T., Silman A.J., et al. (September 2010). 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative // Ann. Rheum. Dis. 69 (9): 1580–8. doi:10.1136/ard.2010.
9. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines // Guidelines for the Management of Rheumatoid Arthritis. 2002 Update. Arthritis Rheumatism. – 2002. – №46. – P. 328–346.
10. Mastbergen S.C., Jansen N.W.D., Bijlsma J.W. and Lafeber F. Differential direct effects of cyclo-oxygenase-1/2 inhibition on proteoglycan turnover of human osteoarthritic cartilage: an in vitro study. – Arthrit Res Ther 2006; 8: R2 doi: 10.1186/ar1846.
11. Cutolo M., Sulli A., Ghiorzo P. et al. Antiinflammatory effects of leflunomide on cultured synovial macrophages from patients with rheumatoid arthritis // Ann Rheum Dis. 2003. - V. 62. - P.297-302.