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EFFICACY AND SAFETY OF ANTI-INFLAMMATORY TREATMENT IN ANKYLOSING SPONDYLOARTHRITIS

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The aim of the study was to study the clinical and laboratory efficacy and safety of etoricoxib in patients with ankylosing spondylitis (AS).

Material and methods. The study included 40 AS patients aged 18 to 55 ears who were treated in the rheumatology department of the multidisciplinary clinic of the Tashkent Medical Academy. Based on the purpose of the study, the patients were divided into two groups: group 1 - 20 patients received etoricoxib 90 mg 1 tab x 1 times after meals, group 2 - 20 patients received Diclofenac 100 mg 1 tab. x 1 times after meals for 12 weeks.

Conclusion. After 12 weeks treatment taking etoricoxib 90 mg/day. and diclofenac 100 mg/day. in 1/3 patients with AS, the activity of sacroiliitis decreased. The frequency of side effects between etoricoxib and diclofenac did not differ significantly.

Keywords: ankylosing spondylitis, axial spondyloarthritis, sacroiliitis, non-steroidal anti-inflammatory drugs.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line drugs for many inflammatory joint diseases (rheumatoid arthritis, psoriatic arthritis, gouty arthritis, etc.) [1]. These are probably the most widely used drugs in the world [1]. For most diseases, NSAIDs are considered and used as symptomatic agents used to achieve analgesic and antipyretic effects. However, NSAIDs play a special role in the treatment of patients with ankylosing spondyloarthritis (AS). This allows NSAIDs to be used as pathogenetic therapy in spondyloarthritis (including axial spondyloarthritis -axSpA) [2, 3]. In addition, according to the accumulating data, NSAIDs not only suppress inflammation in various structures of the musculoskeletal system, but are able to reduce the development of structural changes in the spine, that is, to slow down the growth of syndesmophytes, possibly by suppressing the activity of pre-

mesenchymal cells of osteoblasts [4-7]. Accordingly, in AS, a number of scientists and doctors recommend NSAIDs not only as "symptom modifiers", but also as "disease modifiers".

However, the accumulated knowledge about NSAIDs does not provide answers to a number of important questions for the treatment of AS, such as: how long and in what regimens the drugs should be prescribed; When to stop and when to continue NYaQD therapy. On the one hand, the nature of the persistent inflammation in AS means that patients with this disease must take NSAIDs for a long time, possibly permanently. On the other hand, the side effects caused by the use of NSAIDs in the gastrointestinal tract (GIT), cardiovascular system, hemostasis, and kidneys [8, 9] significantly limit the possibility of long-term use of these drugs, and the optimal use of these drugs in terms of benefit-risk ratio to determine the path requires a complete study of the different NSAIDs mode [10].

Chronic pain is pain that started relatively recently and lasts for a long time. It is usually associated with tissue damage or certain disease states. It is a severe physical and psychological injury that also increases the rate of complications, prolongs recovery time, and increases medical costs [3,11]. The mechanism of pain is that tissue damage causes the release of inflammatory mediators and pain-causing substances, thereby activating peripheral nociceptors, and then sending nociceptive signals through receptors to the thalamus and cerebral cortex, causing pain [4].

This study mainly examines the most commonly used NSAIDs: etoricoxib tablets and diclofenac sodium capsules.

The aim of this study is to investigate the clinical-laboratory efficacy and safety of Etoricoxib in patients with AS, including axSpA.

Material and methods. The study included 40 patients aged 18 to 55 years who were treated with AS in the rheumatology department of the multidisciplinary clinic of the Tashkent medical academy. An informed consent letter for participation was a criterion for inclusion in the study.

All patients met the ASAS criteria for axSpA [11]. Twenty-four (60%) patients had bilateral sacroiliitis stage II or unilateral sacroiliitis stage III-IV according to radiographic findings [12]; These patients met the modified New York criteria for AS [13]. 16 (40%) patients had evidence of osteitis on magnetic resonance imaging and no evidence of sacroiliitis on radiography [14]. All patients had a high activity of axSpA — ≥4 according to the BASDAI index (the Bath Ankylosing Spondylitis Disease Activity Index). The study included patients who had not previously taken NSAIDs, as well as subjects who had taken NSAIDs intermittently (courses of less than 14 days) or at doses lower than those recommended for the drug on a continuous basis.

Based on the purpose of the study, the patients were divided into two groups: group 1 - 20 patients received etoricoxib (Koxikea) 90 mg once daily after meals, and group 2 - 20 patients received diclofenac 100 mg once daily after meals for 12 weeks.

To determine the effectiveness and safety of treatment. Treatment efficacy was assessed at 1-4 and 12 weeks. To evaluate the effectiveness of the treatment, to determine the changes in axSpA activity indices (BASDAI [10], AS disease activity index - ASDAS [11]), the dynamics of laboratory parameters were studied - the level of erythrocyte sedimentation rate according to Westergen (ESR) determined by a highly sensitive immunophotometric method using Diasis reagents and C-reactive protein (CRP) levels. ASAS20, ASAS40 and partial remission ASAS, the number (%) of patients who achieved a response of 50% reduction in BASDAI index (BASDAI50) were considered [12]. PASS (the Patient Acceptable Symptom State) and PhASS (the Physician Acceptable Symptom State) indices were evaluated to assess patient and physician satisfaction [13].

The safety of the treatment in the 1st, 4th and 12th weeks, taking into account the number of side effects (SE), general condition and control of vital functions (heart rate, respiratory rate, arterial pressure, etc.), laboratory indicators - general blood analysis, general urine analysis, total bilirubin and its fractions, aspartate and alanine

aminotransferases, γ-glutamyl transpeptidase, alkaline phosphatase, urea, creatinine, and glucose levels were evaluated.

Statistical analysis. Statistical processing of received data Microsoft. Excel was performed using Statistica 6.0. The analysis included generally accepted procedures of descriptive statistics, non-parametric methods of comparison. Each patient signed a consent form to participate in the study. The study was approved by the local ethics committee.

Research results. Description of patients participating in the study.

Indicator	**Koxikea group (n=20)**	**Diclofenac group (n=20)**
Age, in years	30 (24;38)	33 (23;41)
Aks SpA duration, in years	3,5±2,6	3,6±4,6
Age at disease onset, in years	21,2±3,9	23,3±4,4
Men/Women	14/6	15/5
AS/early axSpA	11/9	12/8
Psoriasis	1	0
Uveitis	2	1
Enthesitis	6	5
Peripheral arthritis	6	6
Dactylitis	2	2

The time of action and duration of action of various nonsteroidal analgesics were compared. Etoricoxib tablets have the shortest duration of action and the longest duration of action. Diclofenac sodium capsules have a relatively long onset of action and a long duration of action (Table 1).

Table 1

Comparison of the duration of action of various nonsteroidal analgesics in AS

Characteristics	**Etoricoxib Tablets**	**Diclofenac Sodium Tablets**
onset of effect	30,3±4,6	60,2±5,2*

($\bar{x}$±s, min)		
exposure time ($\bar{x}$±s, min)	62,5±5,7	135,2±12,5*
duration of effect ($\bar{x}$±s, day)	4,98±0,64	4,62±0,78*

Note: *R < 0.05 compared with etoricoxib tablets

Comparison of the analgesic effect of various nonsteroidal analgesics: according to the analgesic effect, as shown in Table 2, diclofenac sodium enteric capsules have the best analgesic effect.

Table 2

Comparison of the pain-reducing effect of various nonsteroidal analgesics ($\bar{x}$±s)

Characteristics	Etoricoxib Tablets	Diclofenac Sodium Tablets
analgesic effect	3,29±0,65	2,51±0,46*

Изоҳ: *P <0,05 эторикоксиб таблеткалари билан солиштирганда

Total score of osteitis activity (TSOA) decreased from 6.5 (4; 9) to 2 (0; 5) points during the study (r<0.0001; n=40). Etoricoxib Tablets 90 mg/day. After 12 weeks, 16 (80.0%) patients who received a dose of osteitis decreased, 2 (10%) patients increased, 1 (5.0%) did not change. A correlation was found between the TSOA achieved as a result of the treatment, the severity of the initial osteitis and the initial ASDAS values: the coefficient Spearman's correlation for the initial osteitis was r=0.773 (p=0.01), and for the ASDAS index - r=0.66 (p=0.019) organized. Thus, the greater the initial disease activity and the initial severity of osteitis, the greater the residual inflammatory changes in the sacroiliac joint (SIJ). No correlation was found between the activity of other clinical and laboratory indicators and the osteitis index score.

Osteitis was completely resolved in 23 (57.5%) patients: in 11 (55%) who took Etoricoxib at 90mg/day and in 12 (60%) who took diclofenac at 100mg/day (p=0.077).

All patients with AS and 4 patients with "nonradiographic" axSpA had signs of fatty degeneration in the SIB at the beginning and end of the study. Out of 6 patients who did not have signs of fatty degeneration at the time of inclusion in the study, 3 foci of fatty infiltration were formed in the area where the osteitis was resolved.

In the process of monitoring the safety of treatment, 5 adverse reactions (ADRs) were recorded: 3 for diclofenac and 2 for etoricoxib. ADRs were characterized by heartburn, appeared after 7 days of continuous medication and stopped after diet correction and omeprazole 20 mg/day capsules were recommended (esophagogastroduodenoscopy revealed no changes in the mucosa of the esophagus and gastrointestinal tract); In 2 patients in the group receiving diclofenac and 2 patients receiving etoricoxib, after 2 weeks of therapy, the increase in the activity of liver transaminases twice the normal level was improved against the background of dietary correction; At week 12, 1 patient in both groups developed insomnia (after sedation therapy ADRs stopped) on the background of emotional overstrain. None of the NTs required drug withdrawal. No serious ADRs were noted.

Summary. 1/3 of patients with axSpA received etoricoxib 90mg/day for 12 weeks. intake diclofenac 100mg/milk. reduces the activity of sacroiliitis in the hip joint. Etoricoxib was not significantly different from diclofenac in the frequency of side effects.

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