Pain Syndrome Removing at Patients with Temporomandibular Joint Disorders and Urinary System

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Abstract

Actuality of using the nonsteroidal anti-inflammatory drugs for complex temporomandibular joint (TMJ) degenerative-dystrophic disorders treatment acquiring further more significance due to increasing of this widespread pathology among the different gender and age of person.Offered results of using the selective cyclooxygenase (COX-2) inhibitors drugorodispersible form of Meloxicam for patient with TMJ osteoarthritis and urinary diseases.Decreasing of the TMJ pain syndrome either during chewing or calm state, jaws activity volume was improved, crackling and crepitation at the joint were decreased.Effectiveness and safety of using the orodispersible tablets of Meloxicam for treatment of TMJ osteoarthritis were estimated.

Index terms— meloxicam, temporomandibular joint, osteoarthritis, urinary diseases.

1 Introduction

iseases of the temporomandibular joint (TMJ) are one of the most common problems of dentistry, maxillofacial surgery. In recent years, a lot of work has been devoted to this subject, which focused on the widespread prevalence of TMJ diseases in people of different sex and age, and the difficulties of their treatment (19,27, **??**1). Degenerative-dystrophic TMJ diseases often occurs in patients with undifferentiated connective tissue dysplasia (CT) based on the background of a variety of concomitant somatic diseases, including the urinary system deseases (up to 49%) (28).

Osteoarthrosis (OA) is a chronic degenerativedystrophic joint disease, based on the degeneration of articular cartilage, which leads to its thinning and a decrease in the amount of cartilaginous tissue, structural changes and exposure of the subchondral bone and the formation of bone enlargements. OA TMJ is a multifactorial disease, factors such as age and genetic predisposition, abnormalities or disruption of the functioning of the joint and surrounding muscles, trauma of the joints or mandible, congenital weakness (CT) of the organism, endocrine diseases, metabolic disorders, autoimmune diseases, etc. (19,28).

OA TMJ is often accompanied by pain, resulting in limited activity, and often in disability, and decreased quality of life of patients (14,24).

In the basis of OA there is an imbalance between the anabolic and catabolic processes in the joint tissues, especially in the hyalin cartilage, where the main pathological changes occur. The main sign of OA is the degeneration of articular (hyaline) cartilage, namely, the inadequate synthesis of chondrocytes of proteoglycans (PG) and the fragmentation of proteoglycan aggregates, which are the most important components of pathological disorders in this disease (26).

Despite the fact that OA is not usually referred to as inflammatory arthropathy, but is considered as a degenerative joint disease, more and more evidence has recently emerged that suggest that inflammation plays a key role in the progression of this degenerative disease (11,15,30).

The result of chronic persistent inflammation in the tissues of the joint and synovitis is the degradation of articular cartilage and remodeling of the subchondral plate of the bone. In this case, the cartilage is thinned,

narrowing the articular crack and forming osteophytes and subhondral cysts. In addition, there is a damage of other tissues of the joint, in particular, the synovial membrane, the articular capsule, intra-articular ligaments, and articular muscles. The leading clinical symptoms of OA TMJ are joint pain, limitation of its functions, and articular sounds (26, **??**1).

The main complaint of the patients with OA TMJ who consult dental surgeon with OA TMJ is pain. The innervation of tissues and facial organs is wide. There is a corresponding area in the cerebral cortex. Patients characterize pain as moderate or severe irradiation, or permanent pain, which increases during movements of the mandible (15,19,20,29).

In the treatment of OA TMJ the clinical picture, the stage of the disease and pain should be taken into account. Treatment is aimed at inhibition of activity of the inflammatory process, prevention of joint degradation, restoration of its function, etc. (19,30).

According to the recommendations of the European Antireumatic League (EULAR), the pharmacological treatment of OA TMJ includes systemic and topical application of nonsteroidal anti-inflammatory drugs (NSAIDs) -selective and nonselective cyclooxygenase-2 inhibitors (COX-2), as well as slowacting chondroprotective drugs (SYSADOAsymptomatic slow acting drugs of osteoarthritis: glucosamine sulfate, chondroitin sulfate, diacerein, avocados / soy noncommunicable compounds), intraarticular injections of corticosteroids and cartilage biopolymers (12, **??**2).

One of the universal groups of drugs are NSAIDs. These drugs occupy a central place in the treatment of pain syndrome in OA TMJ and combine anti-inflammatory, antipyretic, analgesic and antithrombotic properties. NSAIDs reduce the inflammatory process, although most of them (salicylates, ibuprofen, naproxen, tiaprofenic acid) suppress the metabolism of hyaline cartilage, which contribute to the progression of OA (5,21,24).

The advantage of selective COX-2 inhibitors is their stimulating effect on cartilage tissue anabolism by inhibiting the expression of IL 1 and its receptor. These drugs help accelerate the synthesis of growth factors, including the transforming growth factor ? and insulinlike growth factor, inhibit Aggrecan degradation, inhibit cartilage catabolism, neutralize the effect of MMP and reduce the intensity of apoptosis of chondrocytes. Drugs of this group disrupt the synthesis of prostaglandins, reduce the sensitivity of pain receptors to bradykinin, reduce swelling of tissues in the inflammation center, weaken the mechanical compression of nociceptors (1,7,18).

Meloxicam is a selective COX-2 inhibitor, which has a high anti-inflammatory, analgesic and antipyretic activity. It is a derivative of enolic acid, belongs to the class of oxycamines. Due to its selectivity with regard to COX-2 isoenzymes, it has a high gastrointestinal safety profile compared to other drugs of this group (1,22). Compared to other NSAIDs, Meloxicam does not increase the risk of developing heart attack (myocardial infarction), heart failure, arterial hypertension and liver failure (21).

A significant group of negative NSAID reactions is a malfunction of renal blood flow and nephrotoxicity, which appears in the form of fluid retention, hypernatremia, increased serum creatinine levels, and high blood pressure. NSAIDs can induce the development of interstitial nephritis. According to a number of researchers, NSAIDs are the launch of existing conditions that contribute to kidney damage, such as hypertension, chronic pain that is often observed in chronic renal dysfunction (2). On the background of the use of selective COX-2 inhibitors, in particular, Meloxicam, there was no significant increase in the risk of renal insufficiency and its progression in patients with moderate renal insufficiency (clearance of creatinine -20-40 ml/min) (8).

Biological effects of Meloxicam: suppresses the expression of COX-1 and to a greater extent COX-2; suppresses the synthesis of prostaglandins; suppresses the synthesis of leukotrienes; has an anabolic effect; suppresses IL 1?, IL 6, FNP ?; suppresses IL-1mediated production of metalloproteinases (MMP); affects transcription factors, mainly on NF ?B; suppresses the release of lysosomal enzymes; suppresses the production of NO in chondrocytes in both healthy and having OA people (individuals); affects free radicals; inhibits proliferation of synoviocytes; dosedependent stimulates the synthesis of PG and hyaluronic acid (HA); stimulates the synthesis of glycosaminoglycans in cartilage; suppresses the agrikan's degradation; neutralizes the effect of MMP; inhibits apoptosis of chondrocytes (1,23,25).

The pharmacokinetics of Meloxicam: the drug has 99% bind with plasma proteins (mainly albumin), permeability in synovial fluid is 50% compared to plasma, metabolized in the liver almost completely with the formation of four pharmacologically inactive derivatives. Elimination of Meloxicam is mainly in the form of metabolites in equal parts with feces (less than 5%) and urine (small amount). The half-life is 15-20 hours, plasma clearance is an average of 8 ml / min.

Contraindications for the prescription of Meloxicam are: hypersensitivity to Meloxicam or other components of the drug, as well as to active substances with a similar effect, such as acetylsalicylic acid; gastrointestinal bleeding or perforated gastric or duodenal ulcer in the anamnesis; severe hepatic or renal failure; blood coagulation system failure; severe heart failure; treatment of perioperative pain in coronary bypass surgery.

Meloxicam has shown high efficiency and good tolerability in both during intramuscular injections and at oral intake, including patients with OA TMJ with high cardiovascular and gastrointestinal risks (9,24).

In cases when oral administration of drugs in the form of tablets or capsules is difficult for the patient NSAIDs are used in the form of soluble powders (sachets), syrups, orodispersible tablets (ODT) that are dissolved in the oral cavity during a short time (10-30 seconds). Due to this, the amount of the drug subjected to presystemic metabolism or the effect of primary passage through the gastrointestinal tract (GIT) and the liver (4) decreases (compared to a standard solid pill).

Advantages of ODT: convenience of application; the possibility of taking the drug in case when rapid effect is needed; increased bioavailability; the possibility of prescription to elderly patients, as well as other groups of patients who are having difficulty with traditional oral medicine; elimination the risk of strangulation or spasm; improving the perception of the K drug in all groups of patients thanks to its pleasant taste (8,9).

NSAIDs with OA can be used locally, in the form of ointments and gels, and is usually prescribed before oral application of NSAIDs, or in combination with it. The use of NSAIDs locally gives a good clinical effect with a much lower frequency of side effects from the digestive system, but it cannot be compared to the effectiveness of oral forms. To achieve maximum clinical effect, it is recommended to apply ointment locally together with oral forms of NSAIDs (24,27).

2 II.

3 Purpose of the Work

Evaluate the efficacy and safety of Meloxicam in the form of ODT in patients with degenerative-dystrophic TMJ diseases with the background of concomitant urinary tract pathology.

4 III.

5 Materials and Methods

The study involved 38 patients (11 men and 27 women) with OA TMJ, an average age of 45.3 ± 7.6, in which there was a history of concomitant pathology of the urinary system, no allergic reactions to NSAIDs, coagulation of blood, gastrointestinal bleeding or perforation of the stomach; no severe cardiac, hepatic or renal failure. Patients were treated at the Dental Medical Center of the Bogomolets National Medical University and the Department of Nephrology and Hemodialysis of Kyiv City Clinical Hospital ? 3.

Patients were divided into 2 groups: the main group -19 people, comparative group -19 people.

The examination of patients was carried out according to the classic method of examination of patients with TMJ diseases. In the course of this the following were determined: patient's complaints, the cause and duration of the disease, the peculiarities of its course, the presence of concomitant pathology. The objective examination took into account the degree of mouth opening, the volume of movements of the mandible, displacement of the jaw when opening the mouth in one direction or another. Auscultatory the presence of sounds (noises) in the joint was noted. Palpation of TMJ was performed, the presence or absence of pain in the joint and masticatory muscles (temporal, i.e. masseter, pterygoid) was diagnosed.

The severity of the pain was evaluated on the Verbal Descriptor Scale (VDS) scale, according to which: 0 points -no pain, 2 points -weak pain, 4 points -moderate pain, 6 points -severe pain, 8 points -very severe pain, 10 points -unbearable pain (6,13).

Additional methods of the study were orthopantomography with the study of the shape of the mandibular heads, X-ray of the opened mouth by the Parma, MRI of the TMJ. Since patients had a history of an existing concomitant pathology of the urinary system, a nephrologist consultation with ultrasound examination of the kidneys and urinary tract, and urine tests was mandatory.

Anti-inflammatory non-steroidal drugs were being receiving by the patients in for 7 days (main group: Meloxicam in the form of ODT 15 mg / day; comparative group: Nimesulide -200 mg daily), chondroprotectors for 2-3 months (Chondroitin sulfate and Glucosamine hydrochloride -1000 mg daily), combined calcium supplements for 2-3 months (calcium-D3 Nicomed -2 tablets daily, Calceminadvance -2 tablets daily). A thin layer of ointment with anti-inflammatory and warming effect was applied locally 2-3-times a day on the area of TMJ and masticatory muscles. An ointment contained methyl salicylate, camphor, thymol, terpentine and eucalyptus oil. Patients were observed at 7, 21, 30 days of treatment.

6 IV.

7 Results

Among all patients with TMJ diseases included in this study, the nosology of the diseases of the concomitant pathology of the urinary system was as follows: crystalluria (oxalate or urat) -9 (23.7 ± 3.1), nephroptosis -8 (21.1 ± 2, 8%), chronic pyelonephritis -6 (15,8 ± 1,9%), urolithiasis -5 (10,5 ± 1,2%), chronic cystitis -5 (10,5 ± 1,2%), L-shaped kidney -2 (5.3 ± 0.5%), pyelectasia -2 (5.3 ± 0.5%), bladder prolapse -1 (0.5 ± 0.4).

The majority of patients -33 (86.8%) complained of pain in the TMJ. A moderate dull pain at rest was observed in 21 (55.3%) patients according to VDS of 3.47 ± 1.11 points. In these patients, during chewing on solid food or active motions of the mandible, the pain intensified and was 6.09 ± 1.33 points of VDS. Less than half of patients -12 (31.6%) complained of severe TMJ pain only when they opened the mouth and chewed on solid food, which was 6.11 ± 1.22 points of VDS, and no pain was observed at rest.

The duration of the disease from 1 month to 1 year was observed in 15 (39.5%) examined, from 1 to 5 years in 23 (60.5%) patients. In 25 (65.8%) patients, Xray signs of osteoarthritis of the TMJ had been diagnosed, which corresponded to the 1st or 2nd degree of the disease according to the N.N. Kasparov (1981), respectively 16 (42.1%) and 9 (23.7%) patients. The X-ray revealed uneven, indistinct contours of the mandibular heads,

changes in their shape, thinning of the cortical layer, narrowed and uneven articular gap. MRI of the TMJ results showed thinning of the cartilage of the mandibular head and its destruction was observed in 3 (7.9%) persons.

Constraint in the affected joint area was observed in 21 (55.3%) patients, which usually continued from 15 to 20 minutes in the morning, and gradually decreased and disappeared. When opening the mouth, 100% of patients noted the appearance of crepitation or rash in the joint.

During the examination of patients, the restriction of the jaw movements was experienced, in which the opening of the mouth was 3.25 ± 0.86 cm. While opening the mouth, the jaw shift was diagnosed towards to the affected TMJ, crunching or crepitation in the joint, moderate pain when pressed on the chin that took place on the pathological side and according to the VDS was 4.84 ± 1.0 points. Palpation of TMJ and masticatory muscles in most patients was painless -23 (60.5%) patients. In 15 (39.5%) men, trigger points were observed in the anterior parts of the temporal, lower external areas of the masseter muscle, medial pterygoid muscle in the place of its attachment to the inner surface of the mandible. A crunching was noted at vertical, sagittal, transversal movements in the affected joint. Mostly, patients had one-sided lesion of the TMJ.

During a 100% main group study, one week after treatment, it was found that TMJ pain tends to disappear in 10-15 minutes after receiving 1 ODT of Meloxicam 15 mg, which was ± 0.93 of VDS. After 15-25 minutes, the patients observed almost complete reduction of pain at rest -1.58 ± 1.07 points. During chewing, pain remained but became less intense (3.26 ± 0.99 points): in 12 (63.2%) patients the pain was moderate, and 7 (36.8%) patients had mild pain. The duration of anesthetic effect was observed within 1 day; patients did not require re-administration of NSAIDs.

In patients of comparing group on the 7th day of treatment, it was found that pain in the TMJ decreased after 20-30 minutes (2.93 ± 1.01 points) after taking 100 mg of Nimesulide, and a significant decrease (1.47 ± 0.9 points) was marked by patients in 50-60 minutes. The pain during chewing and opening the mouth after an hour was also less intense (3.37 ± 1.16 points) and patients were able to take food without significant discomfort. The duration of the analgesic effect of Nimesulide was observed within 10-12 hours, after which the pain in the TMJ began to increase and patients were forced to re-take the drug.

During repeated visits an increase in the opening of the mouth to 4,02 ± 0,95 cm was noted in patients of both groups, as well as the volume of jaw movements improved, crunching and crepitation in the joint decreased.

In patients of comparison group after 7 days of treatment, most patients noted discomfort in the epigastric area, and 5 people also noted heartburn in the stomach. These patients were prescribed gastro protectors (decoction of flax, Bi?O 120 mg twice a day). On the 5th day of taking of the Nimesulide 2 patients noted aching pain and heaviness in the lumbar area. After the examination and urinalysis modification detection (the appearance of protein to 0.33 g/l and unmodified erythrocytes in sight) it was recommended by the nephrologist to discontinue the drug.

In the main group, Meloxicam in the form of ODT was well tolerated by patients, had no irritating effect on the mucous membrane of the gastrointestinal tract, urinary tract, no allergic reactions. Patients noticed that ODT was pleasing to taste, quickly dispersed in the oral cavity. The pain decreased in 20 minutes and did not occur for a long time, which did not require readministration of NSAIDs during the day. The control of urine tests did not reveal any changes in relation to the initial level. In addition to this, patients indicated a decrease in emotional stress, fear of limiting movements of the mandible, improvement of the general condition of patients.

V.

8 Conclusions

The pain in the TMJ at rest, as well as when opening the mouth and chewing decreased at patients with degenerative-dystrophic diseases of TMJ and concomitant pathology of the urinary tract system during taking Meloxicam in the form of ODT 15 mg daily. The volume of the movements of the mandible improved, the opening of the mouth was 4.02 ± 0.95 cm, crunch and crepitation in the joint decreased.

The drug has an evident pain relief effect that comes quickly and lasting for a long time. ODT Meloxicam is well tolerated by patients, has a pleasant berry flavor, is convenient in use, has no undesirable effects on the digestive tract and urinary system and side effects. The psycho-emotional state of patients was normalized.

Meloxicam ODT can be used in patients to eliminate the pain syndrome in the complex treatment of patients with degenerative-dystrophic TMJ diseases, compared to the receiving of Nimesulide does not cause irritation from the digestive and urinary system. [1]

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