Use of Apizartron Ointment in Combination Therapy of Knee Osteoarthrosis

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ABSTRACT

Aims: To evaluate the effectiveness of Apizartron ointment used in combination therapy of knee osteoarthrosis (OA).

Materials and methods: 28 patients (mean age 56 years, males 17.9%) with radiographic stage I-II gonarthrosis and mean duration of illness of more than 4 years (range 1-8) were treated by combination therapy of NSAIDs, intravenous laser therapy, local magnetic therapy and intra-articular injections of Aprotinin (Contrycal). After 21 days of combination therapy, Apizartron ointment was added to treatment for additional 3 weeks. Arthritic status assessment (by means of visual analog scale, Lequesne index, the WOMAC OA index and symptoms severity evaluation by patient and physician) were performed at baseline, 4- and 12 weeks post-treatment.

Results. Overall, significant improvement was observed in 72% of patients. Patients experienced twice as less knee joint pain and stiffening, range of movement in affected joints has improved considerably. OA severity rate by Lequesne index decreased by 2 degrees, as well as WOMAC OA index. Follow-up after 12 weeks of treatment cessation revealed no deterioration in arthritic status.

Conclusion. Apizartron ointment, used topically in combination therapy of knee OA, proved to be effective, safe medication with long-lasting effect.

Keywords: osteoarthrosis, knee osteoarthrosis, treatment of knee osteoarthrosis, Apizartron ointment.

INTRODUCTION

Osteoarthrosis (OA) is one of the most common diseases of the joints, characterized by the damage of all components of the joint, especially cartilage and subchondral bone, synovium, ligaments, capsule and periarticular muscles [1]. OA is a major cause of disability in older people. The most prominent clinical picture is observed at the age of 55-65.

Knee is the most commonly and early affected articulation due to its position as the support joint, which has to deal with major axial load. Even during a slow walk the knee joint is loaded with a weight 4 times
exceeding the mass of the body. The data supports the relevance of the OA therapy problem as the disease affects not only quality of life of older people but also significant part of the working age population [2,3].

According to the modern concepts, OA develops due to imbalance between anabolic and catabolic processes in articular cartilage [4]. To maintain the integrity of the cartilage, the constant synthesis, compensating losses of glycosaminoglycans (GAGs), collagen and hyaluronic acid due to natural metabolism, is required. In pathological conditions increased intensity of cartilage catabolism exceeds the activity of anabolic processes. Synthesis of anti-inflammatory cytokines stimulate production of chondrocytes matrix proteases that lead to collagen and proteoglycans degradation [5,6].

Biochemical and metabolic changes of articular cartilage lead to the deterioration of its biomechanical properties, which adversely affects the underlying bone, causing impairment of the bone balance, increase in intraosseous pressure and development of subchondral sclerosis and osteophytes [2].

Breakdown products of collagen and proteoglycans induce autoimmune response of the body, acting as antigens, which amplifies and supports an inflammation of synovial tissue and further deterioration of articular cartilage [2,5].

Apizartron ointment has 3 major components: apitoxin or honey bee venom, methyl salicylate and mustard oil (allilizoliocyanate). Apitoxin or honey bee venom is the source of many valuable enzymes, amino acids, peptides and proteins. It activates a multistage cascade of reactions in human body, which provides anti-inflammatory, analgesic and bio-stimulating effects. Due to components with anti-inflammatory properties, apitoxin inhibits various stages of the inflammatory process. A significant advantage of peptide components of bee venom over NSAIDs is 10-times higher therapeutic index achieved at very low doses.

Mellitin is considered as the main active ingredient of bee venom, comprising 90% of active peptide complex. At a concentration of 0.3 μg/ml it increases resistance of proteins to thermal denaturation and reduces the severity of the inflammatory response due to the stabilization of lysosomal membranes. Another unique component of bee venom is MSD – a peptide that increases the resistance of endothelium of blood vessels, reducing their sensitivity to inflammatory agents. Aforementioned peptides of bee venom have analgesic effect, inhibit the synthesis of prostaglandins, reduce aggregation of blood cells and its viscosity and clotting, reduce cholesterol in the blood serum and increase hemoglobin levels.

Usage of methyl salicylate as a component of the ointment provides fast and efficient delivery of allilizoliocyanate and bee venom to the inflammation localisation. This is especially important in cases of OA in the elderly, who have high demand in pain-relieving medication due to the gnawing joint pain, but the usage of oral NSAIDs is limited thru chronic diseases of the digestive tract.

Allilizoliocyanate is an important component of Apizartron ointment, which has a well-known local irritant effect. Allilizoliocyanate significantly enhances local blood flow, promotes activation of metabolic processes, increasing the flow of oxygen to tissues and removal of metabolites from the source of inflammation when applied to the skin. Increase in blood flow and high rate of enzyme reactions causes thermal effect, accelerating decay of not sufficiently oxidized metabolites and mediators of inflammation and pain [8].

Thus, Apizartron ointment containing bee venom, allilizoliocyanate and methyl salicylate has effective impact on all stages of the inflammatory process. This effect has sustained and continuous nature and it is achieved by topical application of active ingredients ensuring the absence of systemic side effects.

The aim of this study was to evaluate the Apizartron ointment’ effectiveness for topical therapy of the knee OA.

MATERIALS AND METHODS

28 patients with knee OA, mean age 56 years (range 40-70), males 17.9%, were enrolled in the study. Mean duration of the disease was more than 4 years (range 1-8).
Knee OA was diagnosed via clinical and radiographic data. 18 patients had bilateral disease, remaining 10 patients - unilateral. 20 patients had radiographic stage II condition by Kellgren – Lawrence method, 8 patients – stage I.

The initial state and dynamics of OA symptoms were assessed both before treatment and after cessation using following methods: the index of pain in accordance with visual analog scale (VAS), the index of the gonarthrosis severity (Lequesne) and WOMAC index. OA severity was assessed (in VAS points) by patient and physician. Also, need in taking NSAIDs was evaluated.

All patients received initial combination treatment including NSAIDs, intravenous laser therapy, local magnetic therapy and intra-articular injections of Aprotinin (Contrycal) for 21 days, followed by inclusion of Apizartron ointment for additional 3 weeks.

Method of administration: Strip of ointment of 3-5 cm in length has to be distributed over affected area as a layer of about 1 mm in sickness and left for 2-3 minutes until the response to the drug application (redness, feeling of warmth) is achieved, then slowly and intensely rubbed into the skin. Apizartron ointment was used 2 - 3 times per day for three weeks.

### RESULTS

At baseline, majority of patients had significant gonarthrosis Lequesne index (average VAS score 6.0), 21 patients – severe level of pain by VAS score (5.0-9.0 cm), remaining 7 - moderate level (3.1-3.9 cm). Patients assessed their overall disease status 6.0 points by VAS, the doctor at 5.0 points.

After 4 weeks of treatment these parameters were re-evaluated. Pain and stiffness rates were the most significantly altered: VAS pain score has reduced significantly, as well as pain stiffness by WOMAC index subscale. Less pronounced changes were achieved in function subscale and total WOMAC index. The severity of gonarthrosis by Lequesne index decreased by 2 degrees, from severe to significant (Table 1).

12 weeks post-treatment with Apizartron, the arthrologic status was re-assessed in terms of abovementioned parameters. Overall, average VAS pain score and subscale WOMAC index remained reduced, severity of gonarthrosis decreased by 2 degrees. Thus, significant improvement in functional status and pain reduction was observed in 72% of patients, status of 4 patients remained unchanged.

### Table 1. Dynamics of arthrologic status indicators in patients with OA 4 and 12 weeks post-treatment using Apizatron ointment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before treatment</th>
<th>4 weeks post-treatment</th>
<th>12 weeks post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. VAS pain score, cm</td>
<td>6.0</td>
<td>3.0</td>
<td>4.9</td>
</tr>
<tr>
<td>2. Lequesne index, score</td>
<td>12.1</td>
<td>7.1</td>
<td>8.1</td>
</tr>
<tr>
<td>3. WOMAC index, score</td>
<td>99.6</td>
<td>52.5</td>
<td>76.4</td>
</tr>
</tbody>
</table>

### Table 2. Assessment of OA dynamics and the need in NSAIDs by patient and doctor

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before treatment</th>
<th>After 4 weeks</th>
<th>After 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment by patient, score</td>
<td>6.34</td>
<td>3.85</td>
<td>5.84</td>
</tr>
<tr>
<td>Assessment by doctor, score</td>
<td>5.04</td>
<td>3.95</td>
<td>4.84</td>
</tr>
<tr>
<td>Number of patients who need NSAID</td>
<td>52</td>
<td>40</td>
<td>20</td>
</tr>
</tbody>
</table>
Table 2 demonstrates the assessment of OA dynamics by patients and doctor, as well as the need in taking NSAIDs. According to the patient assessment, after using Apizartron, OA symptoms were experienced twice as less. Much the same pattern was observed in the evaluation by physician. The need in taking NSAIDs in 60% of patients decreased twice, and 40% of patients were able to stop taking NSAIDs completely.

The least pronounced effect was observed in 4 patients with disease duration of more than 7 years and marked radiologic changes. Further use of Apizartron ointment in this group of patients over time has shown at least stabilization of OA status.

CONCLUSION

NSAIDs are the cornerstone medications in therapy of knee OA, but they have severe adverse effects. Thus, usage of Apizartron ointments in combination therapy has pathogenetic reasoning. Topical use of Apizartron ointment after 21-day course of baseline combination therapy reduces pain and stiffness, improves functional status of the knee in 72% of patients. Owing to introduction of Apizartron ointment, 60% of patients could reduce their daily dose of NSAIDs, and 40% stopped using them. No adverse effects of Apizartron ointment were observed.

REFERENCES: