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Evaluation of the Cartinorm Use in the Therapy of Patients with Knee Osteoarthritis

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ABSTRACT

Background: Knee osteoarthritis is the most common rheumatic disease characterized by pain, structural changes and impairment of quality of life. This disease has a multifactorial etiopathogenesis, and the main role is attributed to mechanical factors. There is a primary and secondary form of osteoarthritis. Osteoarthritis diagnosis is carried out on the basis of history, clinical picture and radiological examinations. Osteoarthritis is a major cause of absenteeism for middle-aged people. In the treatment of osteoarthritis, the triad is important: education, rehabilitation and supportive therapy with chondroprotective drugs. As part of the study, 60 patients with clinical and radiographic signs of knee osteoarthritis were given Cartinorm (1500mg glucosamine sulfate, 800mg chondroitin sulfate, 5000mg forti gel, 250mg vitamin C). After 3 months of treatment, there was an improvement in movement, a reduction in pain and an improvement in activities of daily living as measured by the Oswestry score. **Objective**: The aim of this study was to evaluate the reduction of pain, improvement of the clinical picture and improvement of the quality of life, after three months of supportive therapy with chondroprotective drugs (Cartinorm -1500mg glucosamine sulfate, 800mg chondroitin sulfate, 5000mg forti gel, 250 mg vitamin C). **Methods:** In a study that is prospective, analytical and descriptive, 60 subjects of both sexes with clinical and radiological signs of knee osteoarthritis were included. The study was conducted in six cities (Sarajevo, Tuzla, Banja Luka, Mostar, Zenica and Bijeljina) and lasted three months. During the study for pain relief, patients could only use Paracetamol and all patients took Cartinorm 1x a day. Pain Scale and Ostwestry index tests were performed for each patient to assess the quality of life at the beginning of the study, at the end of the first, second and third month. Results and **Results:** Total number of 60 subjects with clinical and radiological signs of knee osteoarthritis were included in the study. The analysis of the gender structure showed the dominance of the female gender (43 respondents), compared to the male population (17 respondents). The largest number of respondents had bilateral knee osteoarthritis. Assessment of pain through the VAS pain scale on the first day and at the end of the 3-month study showed a statistically significant reduction in pain. Analysis of the quality of life at the beginning of the study showed that 22 subjects performed activities with many difficulties, and at the end of the study only 5 subjects performed activities with many difficulties, which shows an improvement in the quality of life after 3 months of taking Cartinorm. **Conclusion**: Proper education of subjects with knee osteoarthritis and application of chondroprotective drugs (Cartinorm) for a period of 3 months showed an improvement in terms of pain reduction measured through the VAS scale, improvement of knee mobility and improvement of quality of life measured through Oswestry Scor.

Keywords: Knee osteoarthritis, rehabilitation, symptomatic chondroprotectants (Cartinorm) and patient education.

1. BACKGROUND

Knee osteoarthritis is the most common rheumatic disease characterized by: pain, structural changes and dysfunction that later leads to a deterioration in the quality of life (1-3). Osteoarthritis is a disease that affects the synovial membranes and is characterized by

Demographic structure of respondents		Gender					
		Male		Female		Total	
		N	%	N	%	N	%
Age	20–45 years	1	1.7	2	3.3	3	5.0
	46–59 years	7	11.7	18	30.0	25	41.7
	60–69 years	5	8.3	14	23.3	19	31.7
	Preko 70 years	4	6.7	9	15.0	13	21.7
Occupation	Office worker	7	11.7	12	20.0	19	31.7
	Physical worker	4	6.7	9	15.0	13	21.7
	Pensioner	6	10.0	22	36.7	28	46.7
Knee osteoarthritis	Unilateral left	5	8.3	3	5.0	8	13.3
	Unilateral right	1	1.7	12	20.0	13	21.7
	Bilateral	11	18.3	28	46.7	39	65.0
Comorbidity	Yes	14	23.3	35	58.3	49	81.7
	No	3	5.0	8	13.3	11	18.3
Physical treatment	1 time	4	6.7	15	25.0	19	31.7
	2 times	5	8.3	12	20.0	17	28.3
	3 and more times	8	13.3	16	26.7	24	40.0

Table 1. Demographic structure of respondents. x2=0.14 (p=0.990)

the loss of cartilage and the formation of osteophytes (4, 5). There is a primary and secondary form of osteoarthritis. The frequency of osteoarthritis is higher in men up to 50 years old and in women over 55 years old. Within the clinical picture, we distinguish three stages of knee osteoarthritis: first stage – early osteoarthritis; second stage – mild osteoarthritis; third stage – advanced osteoarthritis. The diagnosis of knee osteoarthritis is based on anamnesis, clinical examination and radiological examinations. Kellgren and Lawrence determined four degrees according to the NICE recommendations for the treatment of the severity of osteoarthritis. The frequency of osteoarthritis leads to increased absenteeism among the working population. Patients with knee osteoarthritis have a reduced quality of life, which represents the subjective experience of their own life in relation to the psychological, social and physical well-being of a person and his ability to perform common everyday tasks. The basic triad in the therapy of patients with osteoarthritis are: patient education, rehabilitation and supportive therapy. The therapeutic guide OARS (Osteoarthritis Research Society International) recommends the use of tens, ultrasound and laser in the rehabilitation of patients with knee osteoarthritis, with the highest level of evidence. Recommendation EULAR (European Society for osteoarthritis) and ARC (American College of Rheumatology) recommend the use of slow-acting drugs for a minimum duration of three months. As part of a multicenter, prospective and destructive study, patients with knee osteoarthritis were given Cartinorm (1500mg glucosamine sulfate, 800mg chondroitin sulfate, 5000mg forti gel, 250mg vitamin C) to patients with knee osteoarthritis. At the end of the first, second and third month, the Pain Scale (VAS) tests and assessment of the quality of life with osteoarthritis (Oswestry) were performed.

2. OBJECTIVE

The aim of this study was to evaluate the reduction of pain measured by the VAS scale, the improvement of the clinical picture and the improvement of the quality of life measured by the Oswestry index, after three months of supportive therapy with chondroprotectants (Cartinorm–1500mg glucosamine sulfate, 800mg chondroitin sulfate, 5000mg forti gel, 250 mg vitamin C)

3. MATERIAL AND METHODS

The study included 60 persons of both sexes with clinical and radiological signs of knee osteoarthritis. The study was conducted in six cities (Sarajevo, Tuzla, Banja Luka, Mostar, Zenica and Bijeljina) and lasted three months. During the study for pain relief, patients could only use Paracetamol and all patients took CratiNorm 1x a day. The Pain Scale (VAS) and Oswestry index evaluations were performed for each patient at the beginning of the study, at the end of the first, second and third month.

4. RESULTS

The multicenter study included 60 respondents, of both sexes, 10 from each of six different cities in Bosnia and Herzegovina. The total number of respondents is 60, of which 43 are women and 17 are men, with the average age of women (M=61.64) and men (M=60.11) years. The patients used Cartinorm supportive therapy once a day for a three-month period.

In the study, the dominance of the female population in relation to the male population was established 43:17. In relation to age, the largest number of patients of both genders is between the ages of 46 and 59 in 25 (41.7%) of cases, of which 7 (11.7%) are male and 18 (30%) are female. Based on the chi-square test, no statistically significant difference was found in the relationship between gender and age of the respondents. The largest number of respondents, 39 (65%), has bilateral knee osteoarthritis joint. Comorbidities are present in 49 (81.7%) patients, and 24 (40%) patients have received physical therapy 3 or more times so far.

The mean value of BMI for men is (M=30.4) and for women (M=27.4).

Assessment of pain by the VAS pain scale at the beginning of the study (7) shows a statistically significant

Therapeutic effect on the degree of disability		Age									
		20–45 years		46–59 years		60–69 years		above 70 years		Total	
		N	%	N	%	N	%	N	%	N	%
Oswestry-first month	Activities can be performed without any difficulties	2	3.3	8	13.3	0	0.0	0	0.0	10	16.7
	Activities can be performed with less pronounced difficulties	1	1.7	12	20.0	6	10.0	6	10.0	25	41.7
	Can perform activities with great difficulty	0	0.0	4	6.7	11	18.3	7	11.7	22	36.7
	Activities cannot be performed	0	0.0	1	1.7	2	3.3	0	0.0	3	5.0
Oswestry-second month	Activities can be performed without any difficulties	2	3.3	10	16.7	4	6.7	2	3.3	18	30.0
	Activities can be performed with less pronounced difficulties	1	1.7	14	23.3	9	15.0	11	18.3	35	58.3
	Can perform activities with great difficulty	0	0.0	1	1.7	6	10.0	0	0.0	7	11.7
	Activities cannot be performed	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Oswestry-third month	Activities can be performed without any difficulties	3	5.0	17	28.3	9	15.0	3	5.0	32	53.3
	Activities can be performed with less pronounced difficulties	0	0.0	7	11.7	6	10.0	10	16.7	23	38.3
	Can perform activities with great difficulty	0	0.0	1	1.7	4	6.7	0	0.0	5	8.3
	Activities cannot be performed	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 2. Therapeutic effect on the degree of disability in relation to age

reduction in pain after three months of taking Cartinorman (VAS–3). Analysis of the Oswestry Score and quality of life in patients with osteoarthritis showed that 22 subjects (36.7%) performed daily activities with many difficulties at the beginning of the study. After three months of taking Cartinorm, the same activity of daily life, which includes daily activity with many difficulties, was present in 5 subjects, which shows an improvement in the quality of life.

5. DISCUSSION

One of the most controversial areas in the treatment of knee osteoarthritis is the use of glucosamine and chondroitin. In recent years, three major studies were published in which their influence was studied. Martel-Pelletier and colleagues studied structural changes (radiologically measured by loss of joint space width) and cartilage volume (measured by MRI) in a sample of six hundred patients with knee osteoarthritis, who took conventional drugs, glucosamine/chondroitin sulfate, or both for twenty-four months. Regardless of taking or not taking analgesics/NSAIDs, patients who took glucosamine/chondroitin had a less pronounced decrease in cartilage volume in the medial part of the knee, measured by quantitative magnetic resonance, which was more pronounced in the group with less narrowing of the joint space, or in those with moderate with a serious illness (1).

In a multicenter, double-blind study, Hochberg et al. compared the efficacy and safety of the combination of chondroitin sulfate (CS), 400 mg, and glucosamine hydrochloride (GH), 500 mg three times a day compared to celecoxib (200 mg) once a day in patients with knee osteoarthritis and moderate to severe pain. Patients could take paracetamol as an "exit" drug, but not 24 hours before the evaluation. In a sample of 606 patients, after six months of treatment, a comparable effectiveness of the CS+GH combination with celecoxib was found in reducing pain, stiffness, functional limitations and joint swelling/effusion. (2) The study showed good results as well as our multicenter study. Proven successful therapeutic effect in the functionality of the knee joint. In our study, through a three-month suporative therapy, a reduced degree of disability in activities of daily living was determined, followed by a degree of pain reduction in patients with knee osteoarthritis joint with a statistically significant difference at the beginning and end of treatment.

A subanalysis of that study presented at the OARSI Congress in 2015 indicates that the combination of chondroitin sulfate and glucosamine hydrochloride is more effective in reducing the biomarker Coll2-, a peptide component of collagen type II, compared to celecoxib, in patients with an advanced stage of the disease (stage III according to Kellgren- Lawrence), in patients with synovitis, which includes at least one thickened joint or joint effusion event, in patients who have a good response according to the OMERACT-OARSI criteria, or in patients who have a lower pain level on the WOMAC scale (3).

The third study on glucosamine and chondroitin is

that of Fransen et al., who compared the effect of glucosamine (1500 mg/day) and/or chondroitin (800 mg/day) preparations compared to placebo in a double-blind randomized study of 605 patients with mainly early knee osteoarthritis to the narrowing of the joint space. After two years of follow-up and adjustment in relation to other factors, the patients who took the combination of glucosamine and chondroitin had significantly less pronounced narrowing of the width of the joint space compared to the group of subjects who received a placebo. In all groups, a reduction in pain was found, which at the end of the study was not statistically significant, with a note that the patients could additionally take analgesics/NSAIDs (4).

Symptomatic slow-acting drugs used in the therapy of knee osteoarthritis ensure relief of symptoms in patients by acting on the mechanism of pathological changes in the joint, but with fewer side effects. This group can be divided into cartilage matrix precursors (glucosamine, chondroitin sulfate and hyaluronic acid) and cytokine modulators (diacerin) as well as other types of drugs such as bisphosphonates. By their action, they should delay or stabilize the pathological changes in the affected knee, stopping the progression of the disease. Glucosamine is an endogenous amino monosaccharide and a metabolic precursor of glycosaminoglycans, which are a component of the extracellular matrix of cartilage.

The main purpose of therapeutic supplementation is to compensate for the viscoelasticity of the synovial fluid due to inflammation and to protect the cartilage from deterioration. It acts as an inhibitor of the production of metalloproteinases, chemokines and prostaglandins and in this way realizes its biological function in stopping joint degradation.

A systematic review and network meta-analysis lasting 12 months or longer showed that the use of glucosamine sulfate was associated with a reduction in pain intensity as well as an improvement in knee function (5). Zhu et al. observed greater benefits for pain relief and improvement of joint function when using chondroitin compared to placebo (6). A meta-analysis from 2018 concludes that supplementation with glucosamine or chondroitin sulfate reduces pain intensity measured by the visual analog scale (VAS), but does not lead to changes in pain intensity, function, and joint stiffness measured by the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) scale (7).

The different outcomes of research into the effects of symptomatic slow-acting drugs in osteoarthritis may also be a consequence of the different quality of glucosamine and chondroitin sulfate preparations. This has been researched and a 2020 meta-analysis shows that chondroitin sulfate and crystalline glucosamine sulfate of pharmaceutical grade that are registered as a drug are more effective in relieving pain than glucosamine and chondroitin preparations that are sold as dietary supplements and do not have strict quality and purity control as well as sufficient concentration of chondroitin (8). Official guidelines have different views on the use of glucosamine and chondroitin sulfate in knee osteoarthritis. ESCEO guidelines recommend the use of only pharmaceutical-grade, pure chondroitin sulfate and crystalline glucosamine as first-line treatment for symptomatic knee osteoarthritis. It states that it can be used as an independent therapy or in combination with acetaminophen (9). In the new OARSI guidelines, symptomatic slow-acting drugs are not listed as a treatment option for knee osteoarthritis (10). ACR gives a recommendation against the use of glucosamine and chondroitin sulfate due to large differences in the outcome of observed studies and suspicion of uneven publication of results due to this, high placebo effect and unknown mechanism of their action (11). Analysis of various studies where patients with osteoarthritis took chondroprotectants showed a reduction in pain and improvement in quality of life in all studies (12-16). Research in our study obtained similar results and proved that the EULARA recommendation for the use of chondroprotectants in subjects with osteoarthritis is a minimum of three months and has a satisfactory therapeutic effect.

6. CONCLUSION

Proper education of patients with knee osteoarthritis and the use of Cartinorm in patients with knee osteoarthritis joint over a period of three months shows a significant improvement in terms of pain reduction measured by the VAS scale, better mobility, and improvement in activities of daily living measured through the Oswestry index.

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