

## Research Article

# The Clinical and Biochemical Effects of Oral Glucosamine and Chondritin Patients with Knee Osteoarthritis; A Randomized, Single Blinded, Controlled Clinical Trial

Bilge A<sup>1</sup>, Ertürk C<sup>2</sup>, Isikan UE<sup>2</sup>, Altay MA<sup>2</sup>, Öztürk IA<sup>2</sup>, Ulusoy RG<sup>1</sup> and Dogramaci Y<sup>3\*</sup>

<sup>1</sup>Department of Orthopaedics, Kafkas University, Turkey

<sup>2</sup>Department of Orthopaedics, Harran University, Turkey

<sup>3</sup>Department of Orthopaedics, Mustafa Kemal University, Turkey

\*Corresponding author: Yunus Dogramaci, Department of Orthopaedics, Mustafa Kemal University, Hatay, Turkey

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## Abstract

**Objectives:** To determine the effects of the oral glucosamine hydrochloride and chondritin sulphate on the clinical and serological markers of knee osteoarthritis.

**Material and Methods:** The study was conducted during July 2008 - July 2010, 44 patients with age range between 40-70 years were included in the study. Patients were randomly allocated into two groups each with 22 patients. In the first group oral Glucosamine Hydrochloride (GH) and Chondritin Sulphate (CS) were administered orally. In the second group, home exercise and paracetamol oral tablet were applied. Before starting the treatment and after 6 months the blood and synovial cartilage degradation markers including Collagen Type II (CII) and C-terminal Telopeptides of type II collagen (CTX-II) were measured. Clinically the VAS score and the Western Ontario and McMaster Universities (WOMAC) score were used to evaluate the clinical improvements.

**Results:** there was no statistically significant difference between the two group regarding the age, sex, body mass index, radiologic staging and clinical evaluation ( $p>0.05$ ). Also there was no statistically significant difference between the study and control groups regarding the biochemical markers of osteoarthritis before and after 6 months of the treatments ( $p>0.05$ ). Clinically, there was statistically significant improvement in the VAS and the (WOMAC) scores in the study group whereas no significant change was observed in the control group.

**Conclusion:** In patients with knee osteoarthritis, oral glucosamine hydrochloride and chondritin sulphate improves clinical symptoms however it has no effects on the biomechanical markers of osteoarthritis.

**Keywords:** Knee; Glucosamine; Chondritin; Osteoarthritis

## Introduction

Osteoarthritis characterized by progressive destruction of articular cartilage with changes in the subchondral bone, osteophyte formation and sclerosis may be secondary to genetic, mechanical and biochemical factors [1-3].

Among the synovial joints, knee joint is the most commonly affected with symptomatic osteoarthritis. The mainstay of managing knee osteoarthritis is to maintain range of motion and improve function. This result can be achieved using Non-Steroidal Anti-Inflammatory Drugs (NSAID), physiotherapy, intra-articular medication and surgical treatments [4]. As a result of the short half-life of NSAID and the side effects of these medications there was an increase in the numbers of the studies to find alternative medications and to investigate the pathogenesis of osteoarthritis.

Accordingly the disease modifying agents and or chondroprotective agents were introduced.

Oral glucosamine hydrochloride and chondritin sulphate were

among these disease modifying agents used for treating osteoarthritis. Glucosamine and chondritin are the normal components of the articular hyaline cartilages. Glucosamine is a molecule formed in the body from a simple amine and glucose [5]. The main function is to stimulate the production of glucoseaminoglycan, the basic component in cartilage scaffold [6]. Chondritin sulphate is the main component of the extracellular matrix. It increases the proteoglycan concentration in the peri-cellular matrix of the human chondrocyte cell cultures and decreases the collagenolytic activities in the same medium [7]. In osteoporotic patients the bone degradation products will decrease with treatments [8,9].

Oral glucosamine hydrochloride and chondritin sulphate has been shown to decrease the pain and improve the function of joints in previous studies. Furthermore experimental studies in the animals has shown that Oral glucosamine hydrochloride and chondritin sulphate decrease the cartilage degradation [10,11]. The aim of the current study was to investigate the effects of Oral glucosamine hydrochloride and chondritin sulphate on the serum and blood levels of the cartilage degradation products.

## Material and Methods

This study was designed as a prospective, randomized, controlled and single blinded study. During the period between July 2008-July 2010, 44 patients (16 male and 28 female patients) with knee pain of more than 6 months duration were included in the study. All patients had primary osteoarthritis (according to the American romatismal guidelines) [12], and grade 2-3 radiologic osteoarthritis according to the Kellegren-Lawrence staging [13]. The inclusion criteria included the presence of synovial fluid for analysis at the baseline and six months after treatment. The mean age was 52 years (40–70 years). Exclusion criteria were, previous surgery on the lower extremity, any intra-articular injections with the last one year, patients with history of physiotherapy to the knee, any central or peripheral neurologic disease, and diabetic patients, any history of oral medication within the last year and history of trauma to knee joint.

In the first group (study group n=22), oral glcN HCL 1500 mg/day and CS 1200 mg/day were administered for six months. A standard home exercise program plus parasetamol analgesic treatment was prescribed in addition to the oral chondroprotective agents. In the second group (control group n=22) only home exercise program plus paracetamol analgesics treatment were prescribed for six months

Before starting the treatment and after 6 months the blood and synovial fluid were analyzed for the cartilage degradation markers including Collagen Type II (CII) and C-terminal telopeptides of type II collagen (CTX-II).

Strict sterile technique was used to obtain the synovial fluid from the knee joint. All samples were obtained by the same surgeon who was blinded to the study. Venous blood sample were obtained from the upper extremity for serum analysis.

Clinically the VAS score and the Western Ontario and McMaster Universities (WOMAC) score were used to evaluate the clinical improvements.

### Statistical analysis

Analysis were performed using the SPSS 11,5 (SPSS for Windows 11.5, Chicago, IL) programmer. Q square test were used to analyze the gender difference between the groups. Kolmogorov-Smirnov test were used to analyze the distribution of measurements between the groups. Non-parametric tests were used to compare the groups (Mann Whitney U test). Wilcoxon test were used to compare treatment results before and after the study. Values were presented as median  $\pm$  standard deviation, and minimum- maximum.  $p < 0.05$  value were statistically significant.

## Results

The demographic features of both groups are shown in Table 1. There was no statistically significant difference between the groups regarding the age, sex, body mass index and the radiologic staging. ( $p > 0.05$ ). Also there was no statistically significant difference in the VAS and WOMAC scores between the two groups before starting the treatment protocole ( $p > 0.05$ ).

The clinical and laboratory results are shown in Table 2 and 3. There was no statistically significant changes in the serum and synovial fluids level of biochemical markers of cartilage degradation before and after treatment ( $p > 0.05$ ).

**Table 1:** Patients demographic characteristics (Mann-whitney –U test), (Chi-square test).

	Group (n:22) n (%) (mean $\pm$ SD)	Group (n:22) n (%) (mean $\pm$ SD)	P value
Age (years)	50,5 $\pm$ 6,2 (40-63)	53,5 $\pm$ 7,6 (40-67)	0,431
Male	7	9	0,531*
Female	15	13	
Length (cm)	161 $\pm$ 9,4 (150-188)	162 $\pm$ 4,4 (155-172)	0,972
Weight (kg)	81 $\pm$ 11,8 (62-115)	84,5 $\pm$ 13,2 (56-108)	0,934
BMI (kg/m <sup>2</sup> )	30,5 $\pm$ 3,8 (23-37,4)	32,4 $\pm$ 5,8 (19,8-39,6)	0,549
K&Lscore	3 $\pm$ 0,4 (2-3)	3 $\pm$ 0,2 (2-3)	0.753
Stage 2	8	7	
Stage3	14	15	

**Table 2:** Group 1; Clinical and biochemical evaluation before and after treatment (Wilcoxon test).

	Pre-treatment	Post-treatment	P value
VAS	7 $\pm$ 0,9 (5-8)	4,5 $\pm$ 1,8 (2-9)	0,001
WOMAC	60 $\pm$ 10 (43-81)	45,5 $\pm$ 15,6 (31-77)	0,001
Serum CII	4,7 $\pm$ 7,1 (1-35)	3,6 $\pm$ 5,9 (0,9-24,3)	0,733
Sinovyal CII	3,2 $\pm$ 5,1 (1,2-19,2)	3,5 $\pm$ 13,8 (1,8-64,5)	0,291
Serum CTX-II	111,5 $\pm$ 60,9 (50-258)	80 $\pm$ 120 (40-563)	0,178
Sinovyal CTX-II	113 $\pm$ 123,2 (8-465)	91,5 $\pm$ 152,9 (3-550)	0,673

**Table 3:** Group 2; Clinical and biochemical evaluation before and after treatment (Wilcoxon test).

	Pre-treatment	Post-treatment	P değeri
VAS	6 $\pm$ 1,2 (4-9)	7 $\pm$ 1,5 (4-9)	0,922
WOMAC	63,5 $\pm$ 11,2 (41-81)	65 $\pm$ 13,1 (39-81)	0,715
Serum CII	1,6 $\pm$ 2,1 (0,8-8,4)	1,4 $\pm$ 1,9 (0,8-9,3)	0,330
Sinovyal CII	2,4 $\pm$ 4,7 (1-19,5)	2,8 $\pm$ 5,7 (2-19,6)	0,017
Serum CTX-II	85 $\pm$ 76,2 (38-375)	80 $\pm$ 69,8 (18-318)	0,614
Sinovyal CTX-II	76,5 $\pm$ 146,8 (3-493)	94 $\pm$ 136,7 (13-513)	0,709

There was statistically significant clinical improvement in the study group as shown by both the VAS and WOMAC score ( $p < 0.001$ ). There was no statistically significant changes in the VAS and WOMAC scores in the control group ( $p > 0.05$ ).

## Discussions and Conclusion

This study has shown that the oral GH and CS have no effects on the serum and synovial levels of the cartilage degradation products (CII and CTX-II). Many biochemical markers have been used to predict the treatment effects in osteoarthritis [14]. Type II collagen is the main component of the articular cartilage. The damage to the collagen II structure is the main pathophysiological change in osteoarthritis and studies focused on markers which can show these changes in type II collagen [15-16]. Synovial fluid analysis yields better results regarding the laboratory evidences of osteoarthritis. However the difficulties to obtain the synovial fluids and the effects of the synovial fluid volume on the concentration may make it difficult choice for investigation

Unlike the synovial fluid analysis, the blood levels of biomarker's are relatively unaffected by the volume of the serum as it's relatively stable [17,18]. In our study we used both the synovial and serum for

analyzing the effects of the treatment.

Lohmander et al. were first to estimate the levels of CTX-II in synovial fluids in clinical study [19]. In that study the levels of CTX-II were significantly higher in patients with osteoarthritis, meniscal tear, ACL tear comparing to normal healthy person. Furthermore in the same study they found a significant decrease in the level of CTX-II of patients with acute arthritis and meniscal tear after the treatment. In knee osteoarthritis there was no relation between the radiologic stage and the synovial fluid level of CTX-I.

VAS has been used in previous clinical studies to evaluate the pain level [20]. In our study we used the VAS score to evaluate the changes in the joint pain. There was significant improvement in the VAS score of the study group after the treatment protocol.

Tovvheed et al. in a metaanalysis, including 20 control studies and 2570 patients, has shown that oral GH is an effective method to reduce the pain in osteoarthritis [21]. Our study is in accordance with literature in that we found that oral GH and CS reduced the joint pain effectively.

WOMAC scale is an important evaluator of osteoarthritis. We have used the WOMAC to evaluate the effects of the treatment both functionally and clinically [22]. We found significant improvement in the WOMAC score in the study group. However, no significant change was observed in the control group. Hughes et al. in a clinical study involving 80 subjects, has compared the effects of GH to that of placebo. They found no changes in the WOMAC scale and found no changes [23]. Dudek et al. in another clinical study including 50 patients with knee and hip osteoarthritis has used the oral GH and evaluate the results with WOMAC scale. They found significant improvement in the WOMAC scale in 38 patients (80%) [24].

Only limited studies are available in the literature which evaluates the chondroprotective effects of the oral GH and CS [25-27]. In our study we couldn't find a chondroprotective effect of oral GS and CS.

Biochemical markers show earlier changes in response to treatment comparing to the radiological changes, so it is important to follow the progress of the disease. The chondro-homeostatic and the anti-inflammatory effects of the GH and the CS have been shown separately in the previous studies. However, in our study we used the combination of GH and CS to see the effects of this combination on the blood and the serum levels of CII and CTX-II.

In conclusion the results of this prospective randomized control study shown that oral glucosamine hydrochloride and chondritin sulphate improves the clinical symptoms however it has no effect on the serological and synovial markers of knee osteoarthritis. More studies are required to discover the chondroprotective effects of these agents.

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