The Effect of Oral Glucosamine Sulfate Treatment on Pain, Walking and Daily Activities of Patients with Knee Osteoarthritis

Diz Osteoartriti Olan Hastalarda Oral Glukozamin Sülfatın Ağrı, Yürüme ve Günlük Yaşam Aktiviteleri Üzerine Etkisi

Sibel Mandıroğlu, Halil Uçan, Şafi Edemci, Aslı Mete Topçuoğlu

Ankara Fizik Tedavi ve Rehabilitasyon Eğitim ve Araştırma Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, Ankara, Türkiye

ABSTRACT

Objective: Osteoarthritis is basically a degenerative disease of joint cartilage and characterized with the change of structure and function of joint. Glucosamine sulfate is a common supportive treatment modality for the osteoarthritis. We aimed to evaluate the short-term effects of daily 1500 mg glucosamine sulfate for 6 weeks on patients with the symptoms of osteoarthritis.

Methods: 100 patients who were diagnosed as osteoarthritis of knee recruited to the study. 50 patients who received glucosamine sulfate, acetaminophen and isometric strengthening exercise for quadriceps femoris were evaluated as glucosamine sulfate group while 50 patients who received acetaminophen and isometric strengthening exercise for quadriceps femoris were evaluated as control group. Body mass index(BMI), "Western Ontario McMaster" WOMAC scores, visual analog scale (VAS), fifty meters walking time, and the ascending-descending time of stair with 10 steps were recorded at the beginning and at the end of the study.

Results: Although there was no difference between the groups for WOMAC scores (GS group 48.26±14.20; control group 48.05±9.58) and VAS (GS group 7.74±1.3, control group 7.20±1.66) at the beginning of study, statistically significant difference was observed at the end of study in favor with the group who received GS (WOMAC score GS group 39.87±9.41,control group 43.08±7.38; VAS GS group 3.22±1.86, control group 5.6±1.78). Fifty meters walking time was not statistically significant between the groups initially, while fifty meters walking time increased significantly in GS group after six weeks.

Conclusion: We suggest that glucosamine sulfate can be considered as an additive nutritional support in addition to the other treatment choices in knee osteoarthritis. *(J PMR Sci 2012;15: 81-5)*

Keywords: Osteoarthritis, glucosamine sulfate, rehabilitation

ÖZET

Amaç: Osteoartrit (OA) eklemin yapısı ve işlevinde değişiklik oluşması ile karakterize, temel olarak eklem kıkırdağının dejeneratif bir hastalığıdır. Glukozamin sulfat (GS), OA için yaygın biçimde kullanılan destekleyici tedavi yöntemidir. Biz bu çalışmada 6 haftalık günlük 1500 mg oral GS'ın diz osteoartritine ilişkili bulguları olan hastalar üzerindeki kısa dönem etkisini araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmaya diz osteoartriti tanısı alan 100 hasta dahil edildi. Oral glukozamin sülfat, asetaminofen ve kuadriseps güçlendirme egzersizi verilen 50 kişi glukozamin sülfat tedavi grubu olarak, asetaminofen ve kuadriseps güçlendirme egzersizi verilen 50 kişi ise kontrol grubu olarak alındı. Girişte ve

Corresponding Author
Yazışma Adresi

Sibel Mandıroğlu
Ankara Fizik Tedavi ve Rehabilitasyon Eğitim ve Araştırma Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, Ankara, Türkiye

Phone.: +90 312 310 32 30
E-mail: sblmandir@hotmail.com

Received/Geliş Tarihi: 27.07.2012
Accepted/Kabul Tarihi: 02.09.2012

çıkışta tüm hastaların vücut kitle indeksleri (VKİ), "Western Ontario McMaster" (WOMAC) skorları, visuel analog skalaları (VAS 0-10), 50 metre yürüme ve 10 basamak merdiven inip çıkma süreleri kaydedildi.

Bulgular: İki grubun giriş WOMAC(GS grup 48,26±14,20;kontrol grup 48,05±9,58) ve VAS ortalamaları (GS grup 7,74±1,3, kontrol grup 7,20±1,66) arasında istatistiksel açıdan anlamlı fark saptanmamasına rağmen, çıkış WOMAC (GS grup 39,87±9,41,kontrol grup 43,08±7,38)ve VAS (GS grup 3,22±1,86, kontrol group 5,6±1,78) ortalamaları arasında istatistiksel açıdan GS grubu lehine anlamlı fark bulundu. Başlangıç 50 metre yürüme süreleri açısından gruplar arasında anlamlı fark saptanmamasına rağmen, 6 hafta sonraki 50 metre yürüme süresi GS grubunda anlamlı olarak azalmıştı.

Sonuç: Glukozamin sülfatın, diz osteoartriti olan hastaların tedavisinde diğer tedavi seçeneklerine ilave olarak verilebilecek faydalı bir nutrisyonel destek olduğu kanısındayız. *(FTR Bil Der 2012;15: 81-5)*

Anahtar kelimeler: Osteoartrit, glukozamin sülfat, rehabilitasyon

Introduction

Osteoarthritis (OA) is basically a degenerative disease of joint cartilage and it is characterized by the change of structure and function of the joint. OA is a disease which causes high social and economic costs; creates progressive arthralgias, and temporary or permanent movement constraint (1). Glucosamine sulfate (GS), which is commonly used for OA, is a supportive treatment method (2,3). It was confirmed that GS is effective in bringing OA symptoms under control in many studies (4,5,6). Despite it was shown that GS clears free oxygen radicals, its mechanism of action has not been clarified yet (7). In this study, we aimed at investigating the short-term effects of oral GS, which is to be taken 1500 mg once daily for 6 weeks, on patients who have symptoms of knee OA.

Methods

For this study, 50 patients (38 women and 12 men; within the age range of 40-80), with complaint of knee pain and who were diagnosed with knee OA were grouped as the GS treatment group; and 50 patients (40 women and 10 men, within the same age range with the treatment group), who were diagnosed with knee OA, were grouped as the control group. The study was approved by etic commitee of hospital and simple randomization method was used. Knee OA was diagnosed by clinical examination (using American College of Rheumatology criteria) and by Kellgren Lawrence radiologic staging system. Patients, who were over 80, who had intraarticular injection to the knee or had physical treatment within 6 months, who underwent hemiplegia, who have polyneuropathy or lumbar radiculopathy at lower limp, who have cognitive dysfunctions, endocrine and metabolic diseases, were excluded from the study. After patients' informed consents had been taken, 50 people, who were applied oral glucosamine sulfate and quadriceps strengthening exercise, were grouped as glucosamine sulfate treatment group; and 50 people, who were applied quadriceps strengthening exercise, were grouped as the control group. Patients in both groups were given 1500 mg of acetaminophen every day. Treatment duration for both of the groups was 6 weeks. Before the treatment; age, gender, duration of pain, the side of painful knee and Kellgren Lawrence radiologic staging of the patients who were taking part in the study were evaluated. Patients' body mass index (BMI), "Western Ontario McMaster" WOMAC total scores, visual analog scales (VAS), 50 meters walking duration and the ascending-descending 10 steps stair were recorded at the beginning and at the end of the study.

Statistical analyses were carried out by using SPSS (Statistical Package for Social Sciences) 11,0 for Windows. Student-t and Mann-Whitney-U tests were used in order to compare the mean of two independent groups. Chi-square test were used to compare independent group ratio. Statistical significance was accepted as $p<0.05$. All results were assessed in 95% confidence.

Results

The mean of age was 61.70±9.15 for the GS treatment group, and 59.20±8.49 for the control group. According to the analysis conducted, no statistical significant difference was seen between the groups for ages (p=0.344). Pain duration was 7.19±5.22 for the GS treatment group while it was 7.70±6.11 months for the control group. In statistical analysis, no significant difference was observed (p=0.354). In terms of BMI, initial BMI was 29.76±4.12 for the treatment group and 29.17±3.78 for the control group. In statistical analysis, no significant difference was observed between the groups (p=0.178).

In terms of the the side of painful knee, in the treatment group, 15 patients (30%) had right, 10 (20%) had left, and 25 (50%) had bilateral knee pain while in the control group, 17 patients (34%) had right, 8 (16%) had left and 25 (50%) had bilateral knee pain. There was not any statistical significant difference between the groups (p=0.200).

When the groups were analyzed in terms of Kellgren Lawrence radiologic evaluation scale, it was found out that in GS treatment group 30 patients (60%) were grade 2 and 20 patients (40) were grade 3 while in control group, 28 patients (56%) were grade 2 and 22 patients (44 %) were grade 3 (p=0.333) (Table 1).

At the beginning of the study, the average WOMAC total score of the GS treatment group was 48.26±14.20, and it was 39,87±9,41 at the end of the study; for the control group, it was 48.05±9.58 at the beginning and 43,08±7,38 at the end of the study. Although there was not statistical significant difference in WOMAC averages of the both groups at the

beginning of the study (p=0.730), there was statistical significant difference after 6 weeks in favor of the GS treatment group at the end of the study (p=0.018).

At the beginning of the study, VAS score of the GS treatment group was 7.74±1.37, and it was 3.22±1.86 at the end of the study; for the control group, at the beginning, VAS score was 7.20±1.66, and it was 5.6±1.78 at the end of the study. Although there was not significant difference between the groups at the beginning (p=0.193), statistically significant difference was observed in terms of the averages at the end of the study after 6 weeks (p=0.012) (table1) (table 2).

At the beginning of the study, 50 meters walking duration of the GS treatment group was 58.56±12.66 seconds, and it was 50.26±10.0 seconds at the end of the study. 50 meters walking duration of the control group was 58.20±16.11 seconds at the beginning of the study, and it was 56.65±14.33 seconds at the end of the study. In terms of 50 meters walking duration at the beginning of the study, no significant difference was observed (p=0.128); however, in the examination 6 weeks after, statistical significant difference was observed in 50 meters walking duration between the two groups (p=0.029).

When 10 steps-stair ascending / descending durations were compared, it was observed that at the beginning of the study, average duration of GS treatment group was 27.59±17.46 seconds, and the duration at the end of the study was 25.15±12.42 seconds; while at the beginning of the study, average duration of the control group was 26.75±7.78, and 26.45±6.37 at the end of the study. Between the two groups, statistically no significant difference was observed in terms of the average of 10 steps-stair ascending/descending duration at the beginning and at the end of the study (p=0.568,p= 0.574) (Table 2).

Table 1. The comparison of age, pain duration, BMI, dominant side, painful side, radiologic gradings, the mean of initial WOMAC, VAS, Time of walking for 50 meters, and time of climbing up and down for 10 stairs in the GS treatment group and control group

	GS treatment group (n=50)	Control group (n=50)	p value
Mean age (year)*	60.70±9.15	60.20±8.49	0.344
Pain duration (month)	7.19±5.22	7.70±6.11	0.354
Body Mass İndex (kg/m²)	29.76±4.12	29.17±3.78	0.178
Painful side	Right :%30 Left : %20 Bilateral: %50	Right : %35 Left : %15 Bilateral: %50	0.200
Kellgren-Lawrence**	Grade 2: %60 Grade 3: %40	Grade 2: %60 Grade 3: %40	0.333
WOMAC TOTAL İnitial mean	48.26±14.20	48.05±9.58	0.730
VAS initial mean (0-10 cm)	7.74±12.66	7.20±15.66	0.193
İnitial mean (time of walking for 50 meters) (sec)	58.56±12.66	58.20±16.11	0.128
İnitial mean (Time of climbing up and down for 10 stairs) (sec)	27.59±17.46	26.75±7.78	0.568

* mean + standard deviation: Mann Whitney U test

Table 2. The mean of terminal WOMAC, VAS, Time of walking for 50 meters, and time of climbing up and down for 10 stairs in the GS treatment group and control group

	GS treatment group (n=50)	Control group (n=50)	p value
WOMAC terminal mean	39,89±12.94	43,01±11.64	0.018
VAS terminal mean (0-10cm)	3.22±1.86	5.6±1.78	0.012
Time of walking for 50 meters (terminal) (sec)	50.26±10.0	56.65±14.33	0.029
Time of climbing up and down for 10 stairs (terminal) (sec)	25.15±12.42	26.45±6.37	0.574

Discussion

Osteoarthritis is the most common disease of musculoskeletal system. It is one of the most important cause of pain and disability in elderly ages. However, the patients with osteoarthritis desire a painless and active life more frequently. So, the treatment of knee osteoarthritis; which is seen as responsible for the continuous pain and physical disability; is seen as a social and economical target in health administration (8,9) .

Acetaminophen is an oral analgesic that should be used primarily in knee osteoarthritis according to current OA practice guideline and if the patients give response, it is the primary symptomatic drug of choice due to its safety and wide use. Glucosamine sulfate is accepted as a nutritional supplement that is used in mid term and long term management of the disease. In a study of Beamont et al , it was shown that GS that was applied for 1 times 1500mg daily for 6 weeks was found more effective than placebo in the treatment of knee osteoarthritis (10). It is emphsized that analgesic effect of orally GS begins after four weeks and the effects on structural changes could be seen after 1 year (11). For all that Ng et al were reported improved WOMAC scores after GS supplementation at the 6 weeks follow up their study (12). In a study of Ciber et al (4) with the patients which have knee osteoarthritis, it was reported that there was no significant difference between GS and control groups. Similarly, McAlindon et al (7) did also not find any difference on pain between the Glucosamine and placebo groups. However, the results of recent meta-analysis' show that GS is effective on all treatment outcomes including joint space narrowing and WOMAC index (8).

Glucosamine sulfate is a physiologic substance that is used by body for the biosynthesis of proteoglycans, and this also explains the safety of GS because it is used by body naturally and its excretion does not cause any adverse affect (1). In the previous studies, the beneficial effects of GS treatment by its safety and efficacy were shown, and this caused increased attention on nutritional therapy methods of osteoarthritis (13).

Glucosamine sulfate is the first agent to be classified as symptom and structure modifying drug in the treatment of OA by authorized scientific institutions (3). The exact mechanism of action of GS has not been established yet. However, recently, some interesting studies on the mechanism of action of GS in the treatment of OA have been published (14,15). GS is accepted as agent has potential to change the disease course in OA (8). The datas supports that GS is a supportive agent modifies the symptoms and cartilage structure in the treatment of OA (16). In the short term clinical experiments, it was shown that some effects which are unrelated with cartilage such as the inhibition of formation of superoxide radicals or inducible synthesis of nitric oxide may explain the rapid initiation of effects on the symptoms. However, the long term effects can be explained by the stimulation of anabolic activities such as synthesis of proteoglycans and inhibition of catabolic activities such as decreasing the effects of metalloproteases (9). Because of these effects, GS ceases the pathological mechanisms that cause joint degeneration, and so delays the progression of disease and relieve the symptoms of OA. Therefore, the therapeutic effects of GS continue despite the cessation (1).

In our study, although there was no significant difference in initial WOMAC averages of two groups, it was seen that there was significant improvement in terminal WOMAC averages in the GS treatment group. Therefore, there was also significant improvement in the terminal VAS scores in the GS treatment group while no difference was present in initial VAS score between the groups. In our study, the patients in the GS treatment group became better that control group on time of walking for 50 meters. However, there was no statistical difference between the groups when they were compared for the time of climbing up and down for 10 stairs. In our study, no adverse effect of GS was determined. It was thought that contribution of possible placebo effect of GS on the patients could not be ignored. For the purpose of evaluation of possible placebo effect of drug, a comprehensive placebo-controlled study should be designed.

In general, GS is a supportive agent that has good tolerability, and it shows positive effect on daily life activities of patients (17,18). We are of opinion that GS can be advised as a nutritional support in addition to other treatment options in the patients with knee osteoarthritis.

References

1. Qiu GX, Gao SN, Giacovelli G, Rovati L, Setnikar I. Efficacy and safety of glucosamine sulfate versus ibuprofen in patients with knee osteoarthritis. Arzneimittelforschung 1998; 48: 469-74.
2. Clegg DO, Reda DJ, Haris CL, Klein MA, O'Dell JR, Hooper MM, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. N Engl J Med 2006; 354:795-808.
3. Pavelká K, Gatterová J, Olejarová M, Machacek S, Giacovelli G, Glucosamine sulfate use and delay of progression of knee osteoarthritis: A 3-year, randomized, placebo-controlled, double-blind study. Arch Intern Med 2002 ; 162:2113-23.
4. Cibere J, Kopec JA, Thorne A, Singer J, Canvin J, Robinson DB, et al. Randomized, double-blind, placebo-controlled glucosamine discontunation trial in knee osteoarthritis. Arthritis Rheum 2004; 51:738-45.
5. Braham R, Dawson B, Goodman C. The effect of glukosamine supplementation on people experiencing regular knee pain. Br J Sports Med 2003;37:45-9.
6. Cohen M, Wolfe R, Mai T, et al. A randomized, double blind, placebo controlled trial of a topical cream containing glukosamine sulfate, chondrotin sulfate and camphor for osteoartritis of the knee. J Rheumatology 2003;30:523-8.
7. McAlindon TE, LaValley MP, Gulin JP, Felson DT. Glucosamine and chondroitin for treatment of osteoarthritis:a systematic quality assessment and meta-anaysis. JAMA 2000; 283: 1469-75.

8. Bruyere O, Pavelka K, Rovati LC, Deroisy R, Olejarova M, Gatterova J, et al. Glucosamine sulfate reduces osteoarthritis progression in postmenopausal women with knee osteoarthritis: evidence from two 3-year studies. Menopause 2004 ;11:134-5.
9. Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, et al. Long-term effects of glucosamine sulfate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. Lancet 2001;357:251-6.
10. Herrero-Beaumont G, Ivorra JAR, Del Carmen Trabado M, Blanco FJ, Benito P, et al. Glucosamine sulfat in the treatment of knee osteoarthritis symptoms: a randomized,double-blind, placebo-controlled study using acetominophen as a side comparator. Arthritis Rheum 2007;56:555-67.
11. Reginster J Y, Bruyere O and Neuprez A. Current role of glucosamine in the treatment of osteoarthritis.Rheumatology 2007; 46: 731-735.
12. Ng NT, Heesch KC, Brown WJ. Efficacy of a progressive walking program and glucosamine sulphate supplementation on osteoarthritic symptoms of the hip and knee: a feasibility trial. Arthritis Res Ther. 2010 ; 12: R25.
13. Mehta K, Gala J, Bhasale S, Naik S, Modak M, Thakur H, et al. Comparison of glucosamine sulfate and a polyherbal supplement fort the relief of osteoarthritis of the knee: a randomized controlled trial. BMC Complement Altern Med 2007; 31: 7:34.
14. Noack W, Fischer M, Förster KK, Rovati LC, Setnikar I. Glucosamine sulfate in osteoarthritis of the knee. Osteoarthritis Cartilage 1994;2:51-9.
15. Largo R, Alvarez-Soria MA, Diez-Ortega I, Calvo E, Sanchez PO, Egido J, et al. Glucosamine inhibits IL-1 beta-induced NFkappaB activation in human osteoartritic chondrocytes. Osteoarthritis and cartilage 2003;11: 290-8.
16. Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, Giacovelli G, Henrotin Y, Dacre JE, Gossett C. Long term effects of glucosamine sulphate on osteoartritis progression: a randomised, placebo-controlled clinical trial Lancet 2001;357: 251-6.
17. Altman RD, Abramson S, Bruyere O, Clegg D, Herrero-Beaumont G, Maheu E, Moskowitz R, Pavelka K, Reginster JY.Commentary:osteoarthritis of the knee and glucosamine. Osteoarthritis Cartilage 2006;14:963-6.
18. Hathcock JN,Shao A.Risk assesment for glucosamine and chondroitin sulfate..Regul Toxicol Phrmacol 2007;47(1):78-83.