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The Use Of Glucosamine In The Treatment Of Osteoarthritis Of Knee: A Randomized ControlledClinical Trial.

Ganesh G Zarekar[1], Paresh P Pawar[2]*, Deepak B Naikwade[3], Vijay K Patil[4], and Shriraj S Bhongale[5].

[1]Assistant Professor, Department of Orthopedics, DVVPF's Medical College, Ahmednagar, Maharashtra, India.
[2]Junior Resident, Department of Orthopedics, DVVPF's Medica lCollege, Ahmednagar, Maharashtra, India.
[3]Professor & Head of Department, Department of Orthopedics,DVVPF's Medical College, Ahmednagar, Maharashtra, India.
[4]Assistant Professor, Department of Orthopedics, DVVPF's MedicalCollege, Ahmednagar, Maharashtra, India.
[5]Junior Resident, Department of Orthopedics, DVVPF's Medical College, Ahmednagar, Maharashtra, India.

ABSTRACT

To determine the effectiveness of glucosamine in reducing pain from osteoarthritis of the knee. A randomized, double-blind controlled study was carried out in a tertiary care medical centre where the patients were treated with either glucosamine 500 mg three times daily or a placebo for 2 months. A total of 120 patients, aged 34 to 81 being treated for osteoarthritis of the knee were included. Pain intensity was measured both at rest and whilewalking as assessed by a visual analog scale at baseline and after30 and 60 days of treatment. There was no statistical difference between the 2 groups in scores on the visual analogscale at 30 days for both resting (mean [SD] score placebo group 0.18 [2.5] vs 0.71 [2.3] glucosamine group, P=0.27) or walking (5.1 [2.6] vs 5.3 [2.4], P=0.69); there was also no difference at 60 days for both resting (3.2 [2.4] vs 3.1 [2.4], P=0.71) or walking (4.7 [2.1] vs 4.7 [2.7], P=0.87). Also there was no statistical difference between groups in the mean changefrom baseline in scores on the visual analog scale (mean [SD] change for walking at 60 days placebo group −1.5 [2.5] vs glucosamine group −1.4 [3.0], P=0.83). Glucosamine was no better than placebo in reducing pain from osteoarthritis ofthe knee in this group of patients.

Keywords: Glucosamine, osteoarthritis of knee, pain

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Corresponding author

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INTRODUCTION

Osteoarthritis is the most common aricular rheumatic disease. There are different treatment modalities to control its symptoms as well as progression. Among the pharmacological approaches, non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for symptomatic relief [1]. However they are associated with concerned side effects questioning and limiting theiruse for the same [2]. During the last few decades, different categories of new pharmacological agents have been proposed to be specifically active in osteoarthritis, either through a direct mechanism of action on the metabolism of the articular cartilage and/or by interfering with the disease processes [3, 4] .Recently, the International League against Rheumatism (ILAR) has produced a classification and set of guidelines for testing some of these drugs, that have been labelled symptomatic 'Slow Acting Drugs in Osteoarthritis' [5].

Glucosamine is an amino-monosaccharide and one of the basic constituents of the disaccharide units of articular cartilage glycosaminoglycans. Roden's in vitro studies [6] showed that exogenous glucosamine stimulated the uptake of 35SOj, a marker of glycosaminoglycan synthesis by the chondrocytes. Later studies demonstrated that glucosamine could increase the synthesis of glycosaminoglycan in cartilage cultures [7] and stimulate in vitro and ex vivo theuptake of asSO~- and of aH-prol~ne by the articular cartilage of the rat femoral head [8, 9] suggesting that glucosamine is able not only to stimulate glycosaminoglycan production, but also the synthesis of proteoglycans as a whole. This conclusion was confirmed by recent dose- response experiments in human chondrocyte cultures [10]. These pharmacological properties are probably supported in vivo by glucosamine elective incorporation in the articular cartilage after systemic administration, as demonstrated by animal pharmacokinetic studies using radiolabeled glucosamine [11, 12]. Some controlled clinical trials have examined the efficacy of glucosamine in treating osteoarthritis [13-17].

Hence, the aim of this trail was to confirm the effectiveness of glucosamine in treatment of osteoarthritis symptoms.

METHODOLOGY

A total of 120 participants were included in the study after obtaining ethical committee approval and taking an informed consent. The study was carried out in a tertiary care medical center. Participants were randomly allocated in a double-blind design to treatment with either 500 mg glucosamine three times daily or a placebo for 2 months Treatment lasted 2 months. Patients who were taking other analgesics were instructed to continue them for the duration ofthe study

Inclusion criteria

- History of osteoarthritis of the knee
- Radiographic findings consistent with the disease.

Exclusion criteria

Patients who had been treated earlier with glucosamine or chondroitin, or both, Those were not ambulatory

Those who had radiographic findings classed as less severe than grade 1

Grading was based on criteria described by Kellgren and Lawrence. Grade0 indicated no arthropathy; grade 4 indicated severe arthropathy. Participants were evaluated at the beginningof study and at 30 and 60 days after starting treatment. Pain intensity was assessed with a visualanalogue scale, comprising of markings upto 10cm. A mark at 0 was classed as “no discomfort” and at 10 cm as “severe discomfort.” Participants completed two visual analogue assessments at each visit, one representing pain intensity while at rest and the other representing pain whilewalking. Side effects were assessed at each visit by asking the patient if they had experienced any changes in their physical symptoms since the previous visit. Side effects were noted on thesame form used for data collection.

Demographic data were compared between groups using an independent Student t test for means (age, baseline visual analogue scores, duration of arthritis) and a z test for proportional data (for example, the percentage taking no steroidal anti-inflammatory drugs). Scores on the visual analogue scale at rest and while walking were averaged, and mean between treatment groups were compared at each visit using a one-

way analysis of variance. Changes in scores from baseline were also computed, and the means were compared using a one-way analysis ofvariance. Statistical significance was set at a =0.05.

RESULTS

Altogether, 120 participants were enrolled in the study. They were well matched with respect to demographic data, arthritis duration, baseline score on the visual analog scale, the concomitant use of analgesics, and radiographic stage (table 1).

The mean (SD) age of participants in the placebo group was 64 (11) years and in the glucosamine group was 63 (12)years . The mean (SD) duration of arthritis in the placebo groupwas 14 (13) years and in the glucosamine group 12 (10) years .No statistical differences noted between the glucosamine group and the placebo group in meanscores for resting and walking at the 30-day and 60-day assessment (mean [SD] score for resting at 60 days: placebo group vs glucosamine group, 3.2(2.4) vs 3.1(2.4) P=0.71; score for walking: 4.7[2.1] vs 4.7 [2.7], P=0.87) (table 2).

There was also no statistical difference between the groups when the mean change in scores from baseline was calculated and compared (mean [SD] change for walking at 60 days: placebogroup −1.5 [2.5] vs −1.4 [3.0] glucosamine group, P=0.83) (table 3).

There was a similar distribution of change in scores at the 60-day assessment for both resting and walking (figures 1 and 2).

Twenty patients (33%) taking glucosamine experienced side effects compared with ten (17%) taking placebo.

The side effects in both the groups were mild and self-limiting, including loose stools, nausea, heartburn, and headache. Side effects subsided after treatmen stopped.

Table 1: Demographic and baseline characteristics of 98 patients with osteoarthritis of the knee who were randomly allocated to treatment with either placebo or 500 mg glucosamine three times daily

Characteristics	Placebo (n=60)	Glucosamine (n=60)	P value
Number of men	60	60	----
Mean (SD) age (years)	64(11)	63(12)	0.64
Mean (SD) duration of arthritis (years)	14(13)	12(10)	0.34
Mean (SD) weight (kg)	91(15)	91(20)	0.88
Mean (SD) score of pain intensity at baseline*:	--	--	--
Resting	3.5 (2.7)	3.7 (2.3)	0.54
Walking	6.2(2.4)	6.3 (2.4)	0.94
Number (%) taking analgesics:	--	---	---
NSAID	18	19	0.99
Acetaminophen	12	10	0.80
Hydrocodone and acetaminophen	3	3	0.99
Number (%) at each radiographic stage:	---	--	--
Grade 1	19	19	0.36
Grade 2	11	12	0.85
Grade 3	20	19	0.71
Grade 4	10	10	0.37

Table 2: Scores of pain intensity as measured with a visual analogue scale*

Mean (SD) score	Placebo	Glucosamine	P value
At 30 days			
Resting	3.7 (2.9)	3.4(2.3)	0.64
Walking	5.2 (2.3)	5.4 (2.3)	0.62
At 60 days			
Resting	3.2 (2.4)	3.1 (2.4)	0.71
Walking	4.7 (2.1)	4.7(2.7)	0.87

Table 3 Mean change from baseline in score of pain intensity as measured with a visualanalogue scale*

Mean (SD) change	Placebo	Glucosamine	P value
At 30 days			
Resting	0.18 (2.5)	0.71 (2.3)	0.27
Walking	1.2 (2.6)	1.1 (2.0)	0.95
At 60 days			
Resting	0.59 (2.9)	0.73 (2.7)	0.77
Walking	1.5 (2.5)	1.4 (3.0)	0.83

DISCUSSION

We found only a little effect on the intensity of pain in patients with osteoarthritis of the knee with glucosamine. A trial of 40 patients with osteoarthritis of the knee found that glucosamine g/day was statistically superior to ibuprofen 1.2 g/day in reducing pain scores at 8 weeks.3 Glucosamine was less effective than ibuprofen when patients were assessed at 4 weeks. The largest study included 252 patients and found that glucosamine 1.5 g/day was superior to placebo in reducing pain score [15]. The patients in the current study were older, heavier and had arthritis from a very long duration, if we compare the characteristics of the patients from other trials. Hence we hypothesized thatpatients with increased diseased severity may not respond well. Glucosamine helps in formation of proteoglycans and these proteoglycans in-turn aids cartilage in retaining their water content and helps in formation of an elastic layer. Cartilage becomes less responsive to any treatment modality as the person ages and this could possibly explain why glucosamine was not very effective in treating osteoarthritis in the present study.

We observed practically no difference between the groups when absolute visual analogue scores were compared. a slight difference in favour of glucosamine when the change in score was compared with the score at rest, however, this did not approach statistical significance.

CONCLUSION

In elderly patients with osteoarthritis of the knee, glucosamine was no better than placebo in reducing the intensity of pain. Long term clinical trials are needed to further substantiate the results.

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