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Research Article

EFFICACY OF CHONDROITIN SULFATE WITH GLUCOSAMINE VERSUS DIACEREIN IN GRADE II AND III OSTEOARTHRITIS KNEE: A RANDOMIZED COMPARATIVE STUDY

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ABSTRACT

Objective: Osteoarthritis (OA), the most common joint disease has led to great morbidity and disability. Symptomatic slow acting drugs for OA, which includes glucosamine sulfate, chondroitin sulfate, and diacerein provides symptom relief and structure-modifying effects in OA knee. Our aim was to assess the efficacy and safety of chondroitin sulfate with glucosamine versus diacerein in Kellgren-Lawrence Grade II and III OA knee patients.

Methods: After approval from Institutional Human Ethics Committee and after getting written informed consent patients were randomized to Group A: Tablet chondroitin sulfate (400 mg) with glucosamine (500 mg) combination thrice a day or Group B: Capsule diacerein 50 mg, twice a day orally both after food. Out of 88 patients screened, 75 of them entered the study. A total of 15 patients failed to complete the study. Remaining 60 patients completed with 30 patients in each group. They were assessed for pain using visual analogue scale (VAS) from baseline and followed-up at 3, 12, 24 weeks.

Results: Baseline characteristics in both the groups were matching without any significant difference. At 24 weeks there was reduction in VAS from 6.76 to 1.96 (71.01%) in Group A and from 6.8 to 3.53 (48.09%) in Group B. There was significant difference between the groups with Group A significant over Group B in VAS. Thus, the effect of drug in Group A on pain reduction was greater than Group B.

Conclusion: The use of chondroitin sulfate with glucosamine combination resulted in improvement in VAS better than diacerein in OA knee.

Keywords: Osteoarthritis, Chondroitin sulfate with glucosamine combination, Diacerein, Visual analogue scale.

INTRODUCTION

Osteoarthritis, (OA) the most common joint disease has led to great morbidity and disability in the community. It is estimated that hip and knee OA as one of the leading cause of global disability. The global age standardized prevalence of knee OA is 3.8% with prevalence higher in females than males [1]. This forms a burden to health care society in all aspects physical, psychological and socioeconomic.

The management of OA includes a combination of non pharmacological interventions and pharmacological treatments [2]. These treatment options focus on the alleviation of symptoms and are only palliative.

Among the pharmacological treatments, non-steroidal anti-inflammatory drugs (NSAIDs) remain the most widely prescribed drugs for OA, despite the fact that they provide only symptomatic relief and do not prevent progression of the disease [3]. Moreover, NSAIDs cause serious adverse effects, especially on long-term use [4]. In this context, there is a need for safe and effective alternative treatments which would provide both symptomatic improvement and disease-modifying effects in OA. Symptomatic slow acting drugs for OA (SYSADOA) provided an answer which includes chondroitin sulfate, glucosamine sulfate, and diacerein [5]. The oral administration of cartilage constituents in patients with OA is thought to make up for the apparent cartilage loss in affected joints.

There are many clinical trials which have proven their safety and efficacy for symptom relief and possible structure-modifying effects [5]. Studies have been conducted individually using either chondroitin sulfate, glucosamine or their combination with NSAIDs or placebo using randomized controlled trials or meta-analysis, but none have compared this combination with diacerein.

Keeping present scenario in mind, a prospective study was planned and conducted by the Department of Pharmacology in Orthopedics Outpatient Departments, Mahatma Gandhi Medical College and Research Institute (MGMCRI) to analyze the efficacy of chondroitin sulfate with glucosamine versus diacerein in OA patients.

METHODS

This was a randomized prospective interventional parallel efficacy study, which was conducted at the MGMCRI Hospital, a rural tertiary care hospital from March 2013 to April 2014. The Institutional Medical Ethics Committee approval was obtained before commencement of this study.

Inclusion criteria were all patients attending outpatient Department of Orthopedics of either sex above 45 years with Kellgren-Lawrence (KL) Grade II and III OA of knee(s). Exclusion criteria were patients diagnosed to have inflammatory arthritis or postraumatic arthritis knee, patients who had previous or ongoing SYSADOA treatment.

The patients who satisfied the inclusion criteria for OA of Grade II and III KL radiological grading [6] were enrolled after written informed consent. A detailed medical history, general physical examination, and local examination of the knee(s) were done and recorded at the time of screening. X-ray knee(s) was carried out at the beginning of the study. The qualified knee(s) were then recorded as the index joint and it was not changed thereafter during the trial.

Patients were assigned to Group A: Tablet chondroitin sulfate (400 mg) with glucosamine (500 mg) thrice a day after food or Group B: Capsule diacerein 50 mg, twice a day orally after food as per randomization tables which were generated using MS Excel with rand function. Allocation concealment was achieved using opaque stacked envelops.

Patients were assessed clinically with visual analogue scale (VAS) along with a radiological assessment of knee(s) at the first visit. The X-ray knee(s) was interpreted by orthopedician. Paracetamol was given for

pain during the initial 1-week. Later on, patient was allowed to take it as and when needed for flare-ups during the study period. The patient was instructed not to use any other concurrent analgesics in any form, oral, injectable or topical. The patients were subsequently followed-up on week 3 (visit 2), week 12 (visit 3), week 24 (visit 4) with VAS assessment for clinical efficacy. The patients were advised to bring the empty blister packs of the medications at every visit to ensure compliance with medication and to report immediately on experiencing any adverse event during the study period. At the last visit of study period (24th week), drug therapy was withdrawn.

VAS was identified as primary efficacy variable. VAS: The patient was asked to indicate the maximum pain experienced in the preceding 48 hrs by putting a short vertical mark on a 10 cm horizontal linear scale graded at 10 mm intervals (0 indicating nil pain and 10 indicating agonizing pain) [7].

RESULTS

A total of 88 patients were screened for eligibility, out of which 75 patients who satisfied the criteria were included in the study and were randomized to either Group A or Group B. A total of 60 patients completed the study while 15 patients failed to complete due to: loss to follow-up (7 in Group A and 5 in Group B) and 3 in Group B discontinued the drug due to diarrhea. The disposition of the patients is provided in the Fig. 1.

Baseline characteristics of the patients are presented in Table 1. There were no significant differences between groups in the baseline parameters. There was no significant difference in baseline values for the efficacy parameters as well. Baseline scores for VAS (6.76±0.73) in Group A were comparable with scores for VAS (6.8±0.41) in Group B.

DISCUSSION

The baseline characteristics of the two groups were matching (Table 1) without any significant difference between the parameters. Mean age in Group A was 50.63 and Group B 51.36. The mean age of all the patients in both the groups was 51. In our study with respect to gender distribution, 22 in Group A and 18 Group B patients were female; 8 and 12 patients were male in Group A and Group B respectively (Fig. 2). Thus, in both the groups out of the total 60 patients, 40 were female and 20 male showing female predominance (66.66%). This shows the tendency of prevalence of OA knee more in females than males which was discussed in a study by Cross *et al*. reflecting the global burden on hip and knee OA [1]. In a meta-analysis done by Srikanth *et al*. have shown that females tend to have more severe knee OA compared to males [8].

The body mass index (BMI) distribution is shown in Table 2. In Group A 21 (70%) patients and 27 (90%) in Group B were overweight; 5 (16.67%) in Group A and 2 (6.67%) in Group B were obese. Overall including patients in both the groups 70% of the patients were overweight and 17% were obese. This shows that higher the BMI more the OA symptoms which was discussed by Tukker *et al*. in 2009 in his study who found a strong association between BMI and OA knee [9].

Table 1: Baseline characteristics of the patients

Parameters	n=30		p value (t/Chi-square test)
	Group A	Group B	
Age, years	50.63±5.94	51.36±4.28	0.59
Gender (F: M)	22:8	18:12	0.27
Weight, kg	65.75±7.61	67.83±5.49	0.23
Height, cm	155±5.55	155.5±5.00	0.68
BMI, kg/m^2	27.38±2.73	28.01±1.65	0.28
KL Grade II	21	22	0.77
KL Grade III	9	8	
Right knee	12	12	
Left knee	9	9	1.00
Bilateral knee	9	9	
Disease duration (years)	2.96±1.22	2.73±1.33	0.48
Diabetes	4	4	1.00
Hypertension	3	4	0.69
VAS	6.76±0.73	6.8±0.41	0.83

N: Number of patients; p<0.05 significant for mean±SD/proportions, SD: Standard deviation, VAS: Visual analog scale, BMI: Body mass index, KL: Kellgren-Lawrence

Table 2: Relationship between BMI and OA

BMI	Number of patients	
	Group A	Group B
Overweight (25-29.9)	21	27
Obese (30-34.9)	5	2
Normal (18.5-24.9)	4	1

BMI: Body mass index, OA: Osteoarthritis

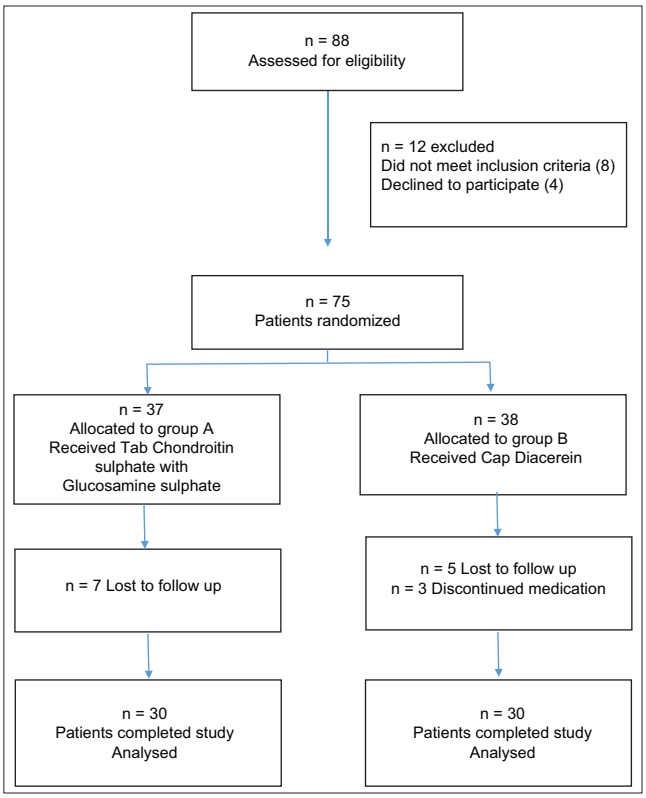

Fig. 1: Flow chart

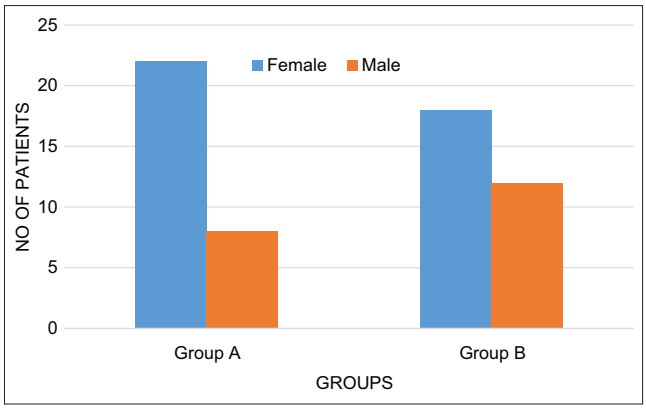

Fig. 2: Gender distribution in groups

Including patients in both the groups 43 (71.66%) out of 60 patients had KL Grade II OA and 17 (23.33) patients had KL Grade III OA. In both the groups the index knee was right, left, and bilateral in 12 (40%), 9 (30%), and 9 (30%) of patients, respectively. Overall right knee was involved more than left knee (40%). The average disease duration in both the groups was 3 years.

The primary efficacy parameter was VAS. The treatment groups had symptomatic OA with the mean VAS score of >6 at baseline. Our study showed improvement in VAS in both the groups during the course of the treatment till 24 weeks i.e., the end of the study.

At 24 weeks, there was reduction in VAS score from 6.76 to 1.96 (71.01%) in Group A and from 6.8 to 3.53 (48.09%) in Group B as shown in Table 3. There was significant difference in VAS scores between the groups detected at 12th week (4.3±0.621) and 24th week (1.96±0.56) in group A with p<0.001 as shown in Table 3. Thus, the efficacy in Group A on pain reduction as assessed by VAS was greater than Group B. These changes in VAS scores in Group A and B are shown in Fig. 3.

The OARSI guidelines 2013 suggest uncertain appropriateness for using SYSADOA in OA knee where uncertain means that it requires a role for physician-patient interaction in determining whether this treatment may have merit in the context of its risk-benefit profile and the individual characteristics, co-morbidities and preferences of the patient [4]. These guidelines diverge from the previous OARSI guidelines in 2010 as well as from recent American College of Rheumatology (ACR) guidelines by focusing specifically on the treatment of OA of the knee. The ACR guidelines 2012 do not recommend the use of SYSADOA [10].

Table 3: VAS scores in Group A and Group B

Duration	Group A	Group B	p value
Week 0	6.76±0.73	6.8±0.41	0.83
Week 3	5.7±0.60	5.8±0.41	0.45
Week 12	4.3±0.61	4.86±0.35	<0.0003*
Week 24	1.96±0.56	3.53±0.51	<0.001*

VAS: Visual analog scale, *p<0.001 statistically significant

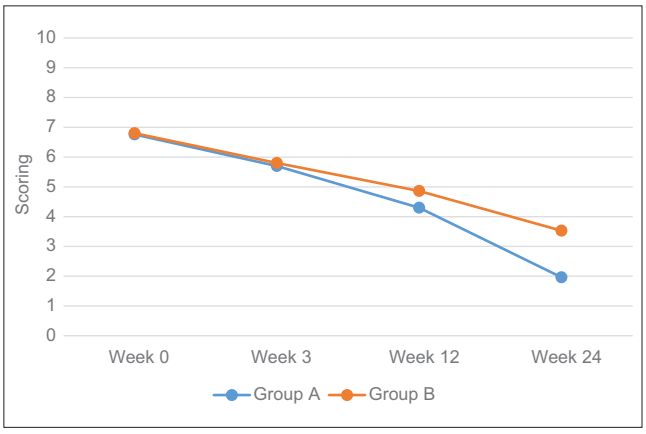

Fig. 3: Change in visual analogue scale scores in Group A and Group B

Irrespective of the differing healthcare policies and treatment standards internationally, our aim should be to identify the best-available treatment practices for knee OA and to implement it to the best of our knowledge acceptable to the patient.

The limitations of our study were small sample size, limited period of study. Thus, further studies with large sample size with long-term follow-up have to be done to confirm the findings of our study.

CONCLUSION

This study indicates that the use of chondroitin sulfate with glucosamine combination resulted in improvement in VAS scores better than diacerein in OA knee. Thus, chondroitin sulfate with glucosamine combination is an effective treatment in OA knee compared to diacerein.

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