

## Comparative Evaluation of Symptom Relief and Disease Modifying Effect of Chondroitin with Glucosamine sulfate and Diacerein in Osteoarthritis Knee

Mirunalini R<sup>1</sup>, Manimekalai K<sup>1</sup>, Chandrasekaran M<sup>2</sup>

<sup>1</sup> Department of Pharmacology,

<sup>2</sup>Department of Orthopaedics,

Mahatma Gandhi Medical

College and Research

Institute, Pillaiyarkuppam,

Pondicherry-607402

### For Correspondence

Dr Chandrasekaran M

Email: chandrortho@yahoo.co.in

Date of

Submission: 11-10-2017

Acceptance: 23-12-2017

Access this article online

Quick Response Code



<https://www.jbcahs.org>

### ABSTRACT

**Background and Objective:** Osteoarthritis [OA] is one of the most common joint disease which has led to great morbidity and disability. Symptomatic Slow acting drugs for osteoarthritis which includes glucosamine sulphate and related compounds, chondroitin sulphate, and diacerein have been found to provide symptom relief and possible structure modifying effects in OA knee. This study compared the efficacy and safety of chondroitin sulphate with glucosamine and diacerein in Kellgren Lawrence grade II & III OA knee patients.

**Material and Methods:** After approval from IHEC and after getting written informed consent, patients were randomized to group A – Tab Chondroitin sulphate (400mg) with Glucosamine (500 mg) combination thrice a day or group B - Cap 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 the study with 30 patients in each group. They were assessed clinically using WOMAC index from baseline and followed at 3, 12, and 24 weeks.

**Results:** Baseline characteristics in both the groups were matching without any significant difference. When compared to baseline at 24 weeks there was reduction in WOMAC from in  $63.5 \pm 4.29$  to  $20.8 \pm 3.19$  (67.24%) in group A and from  $64.3 \pm 3.43$  to  $33.56 \pm 6.03$  (47.81%) in group B. There was significant difference between the groups with group A significant over group B in WOMAC scores with  $p < 0.001$ . Thus the effect of drug therapy on group A was greater than group B.

**Conclusion:** The use of Chondroitin sulphate with Glucosamine combination caused improvement in WOMAC scores better than Diacerein in osteoarthritis knee.

### Keywords:

WOMAC, Diacerein, Chondroitin sulphate, Glucosamine, Osteoarthritis

### INTRODUCTION

Osteoarthritis [OA] one of the most common joint disease has been a burden to the healthcare society both physical and psychological. The reported prevalence of OA in India is 22–39% which accounts for 30% of all rheumatological problems.<sup>1</sup> Indians have a higher incidence of OA of the knee joint, while involvement of the hip joint is less common in comparison to Western populations.<sup>2</sup> This has led to great morbidity and disability in the community

OA can be managed by both non-pharmacological and pharmacological

interventions. The non-pharmacological interventions includes weight reduction, education programs, exercise, and lifestyle changes; pharmacological treatments includes paracetamol, nonsteroidal anti-inflammatory drugs [NSAIDs], topical medication and invasive interventions like intra-articular injections, lavage.<sup>3</sup> These are only palliative and provide only symptomatic relief.

NSAIDs are the most commonly prescribed drugs for OA. They have an advantage of providing symptomatic relief but do not prevent progression

of the disease.<sup>4</sup> NSAIDs also have disadvantages like causing serious adverse effects, especially on long term use.<sup>5</sup> NSAIDs should be considered only in patients not responsive to paracetamol.<sup>6</sup> For these reasons “Symptomatic Slow Acting Drugs for Osteoarthritis” (SYSADOA) which includes chondroitin sulphate, glucosamine sulphate and diacerein which would provide both symptomatic improvement and disease modifying effects in OA was found to be effective and safe in the management of OA.<sup>7</sup>

Chondroitin sulphate and Glucosamine are glycosaminoglycans present in the articular cartilage and plays a major role in the structure and functioning of joints. Hence, products containing these are believed to have positive effects on osteoarthritic joints and to delay the cartilage deterioration.<sup>8</sup> Diacerein is a new anti-inflammatory drug found to act by inhibiting interleukin  $\beta$ (IL $\beta$ ) and it has the advantage of lacking the side effects of classical NSAIDs.<sup>9</sup>

Over the past 10 years the cartilage constituents’ Chondroitin and Glucosamine have been increasingly prescribed by general practitioners and rheumatologists all over the world.<sup>10</sup> Many clinical trials have proven their safety and efficacy along with possible structure modifying effects.<sup>7</sup> Hence this study was planned to analyse the efficacy of Chondroitin sulphate with Glucosamine versus Diacerein in patients with OA

## MATERIAL AND METHODS

This study was conducted in Mahatma Gandhi Medical College and Research Institute, Pondicherry. The study was approved by Institutional Human ethics Committee. Written informed consent was taken from all the study participants.

Inclusion criteria were all patients of either sex above 45 years of either sex with symptomatic OA with Kellgren-Lawrence (KL) Grade II and III<sup>11</sup> OA of knee(s), Exclusion criteria were patients who had previous or ongoing SYSADOA treatment, patients with Inflammatory arthritis or post-traumatic arthritis knee. The patients were enrolled to study after satisfying the inclusion criteria, and signed the informed consent form. At the time of screening a detailed medical history, general physical examination, and local examination of the knee(s) were done. X ray of both knees was carried out at the beginning of the study. The qualified knee(s) were checked and recorded as the index joint.

Patients were randomised using randomization tables generated using MS Excel with rand function. They were allotted to either group A – tablet chondroitin sulphate (400 mg) with glucosamine (500 mg) to be taken thrice a day after food or group B - capsule diacerein 50 mg, twice a day orally after food.

WOMAC Index was used for clinical assessment of the patients. It is a functional assessment scale, which contains 24 questions (Q). For pain (Q1–5), stiffness (Q6–7), and physical function difficulty (Q8–24) pertaining to the knee joint. The response was graded on a qualitative scale (0-none, 1- mild, 2 -moderate, 3 - severe, 4-extreme). The maximum score could be 96.<sup>12</sup>

Western Ontario and McMaster University Osteoarthritis Index (WOMAC) assessment and radiological assessment of knee(s) was done at the first visit. Tablet paracetamol was given to the patients for pain relief during the initial one week of the study period after which patient was allowed to take it as and when needed. Patients were advised to come for follow up on week 3 (visit 2), week 12 (visit 3), week 24 (visit 4) and WOMAC index assessment for clinical efficacy was done. The patients were advised to report immediately on experiencing any adverse event during the study period. At the last visit of study period (24<sup>th</sup> week) drug therapy was withdrawn.

Statistical analysis was carried out using Microsoft Excel 2010. The p value < 0.05 was taken as significant. Data expressed as mean  $\pm$ SD and proportions. Student t test was used to compare data between the groups with respect to their means. Chi-square test was used to compare data between the groups with respect to their proportions

## 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. Fifteen patients were lost to follow-up (7 in group A and 5 in group B) and 3 in group B discontinued the drug due to diarrhoea.

Baseline characteristics of the patients are presented in Table 1. There were no significant differences between groups in the baseline parameters.

**Table 1:** Baseline characteristics of the patients

Parameters	Group A n=30	Group B n=30
Age, years	50.63±5.94	51.36±4.28
Gender(F:M)	22:8	18:12
Weight,kg	65.75 ±7.61	67.83±5.49
Height,cm	155±5.55	155.5±5.00
BMI,kg/m2	27.38±2.73	28.01±1.65
Kellgren-Lawrence Grade II	21	22
Kellgren-Lawrence Grade III	9	8
Right knee	12	12
Left knee	9	9
Bilateral Knee	9	9
Disease duration(years)	2.96±1.22	2.73±1.33
Diabetes	4	4
Hypertension	3	4
Visual Analogue Scale(VAS)	6.76±0.73	6.8±0.41
WOMAC (combined)	63.5±4.29	64.3±3.43

n = number of patients

There were no significant difference in baseline values for the efficacy parameters as well. Baseline scores for WOMAC (63.5±4.29) in group A were comparable with WOMAC (64.3±3.43) in group B.

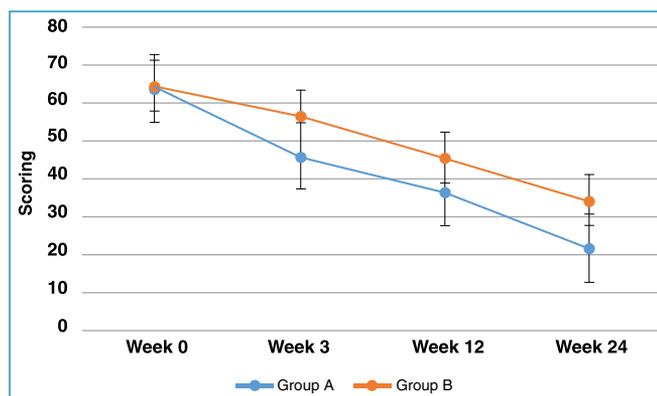
At 24 weeks there was reduction in WOMAC 63.5±4.29 to 20.8±3.19 (67.24%) in group A and from 64.3±3.43 to 33.56±6.03 (47.81%) in group B as shown in table 2. There was significant difference between the groups in WOMAC scores at third week (45.5±4.06) and 24<sup>th</sup> week (20.8±3.19) in group A (p<0.001, Table 2). Thus the efficacy in group A on function improvement with WOMAC scale was greater than group B. These changes in WOMAC scores in group A and B (Figure 1)

**Table 2:** WOMAC scores in the groups

	Group A	Group B	P value
Week 0	63.5±4.29	64.3±3.43	0.43
Week 3	45.5±4.06	56.3±5.17	<0.001*
Week 12	35.86±3.51	44.96±5.72	<0.001*
Week 24	20.8±3.19	33.56±6.03	<0.001*

Values are in mean ± SD ; \*Student t test used.

**Figure 1:** Change in WOMAC scores in the group



## DISCUSSION

SYSADOA have a slow onset of clinical efficacy when compared to NSAIDs and once the administration is stopped they show carry over effect. The main rationale for using SYSADOA is to reduce the use of NSAIDs thereby limiting the risk of upper gastro intestinal track erosions, ulcers and deleterious renal effects in elderly patients.<sup>13</sup>

The treatment groups had symptomatic OA with mean WOMAC score of > 60 at baseline. Our study

showed improvement in WOMAC scores during the course of the treatment till 24 weeks i.e. the end of the study.

The findings of WOMAC scores in group A patients was similar to Glucosamine/chondroitin Arthritis Intervention Trial.<sup>14</sup> The findings of efficacy parameters WOMAC index of diacerein was similar to an Indian study.<sup>15</sup> The same was also discussed in a review of clinical efficacy and safety of diacerein in OA in 2010.<sup>16</sup> The symptomatic benefit provided by diacerein in terms of pain reduction was found to be minimal which was discussed in an earlier Cochrane study.<sup>17</sup>

In contrast to the above findings, Wandel *et al* in his study had shown that chondroitin sulphate and glucosamine did not reduce the joint pain.<sup>18</sup>

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

The limitations of our study were small sample size, limited period of study and lack of a control group.

Thus further studies with large sample size with long term follow up have to be done to confirm the findings of our study.

We conclude that chondroitin sulphate with glucosamine combination is effective in the treatment of osteoarthritis knee compared to diacerein as the combination showed improvement of symptoms and functional disability as assessed by WOMAC index.

## ACKNOWLEDGEMENT

We would like to acknowledge the technical staff and statistician for their support. And also would like to acknowledge the institute for providing financial support.

## CONFLICTS OF INTEREST

None.

## References

1. Ndongo S, Ka MM, Leye A, Diallo S, Niang EH, Sy MH, *et al.* Epidemiological and clinical features of the knee osteoarthritis. *Dakar Méd.* 2003;48:171–5.
2. Sarzi-Puttini P, Cimmino MA, Scarpa R, Caporali R, Parazzini F, Zaninelli A, *et al.* Osteoarthritis: an overview of the disease and its treatment strategies. *Semin Arthritis Rheum.* 2005 ;35:1–10.
3. McAlindon TE, Bannuru RR, Sullivan MC, Arden NK, Berenbaum F, Bierma-Zeinstra SM, *et al.* OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage.* 2014;22:363-88
4. Ullal S D, Narendranath S, Kamath R K, Pai MRSM, Kamath S U, Savur Amarnath D. Prescribing pattern for osteoarthritis in a tertiary care hospital. *Journal of Clinical and Diagnostic Research.* 2010 ;4:2421–6.
5. Chou R, McDonagh MS, Nakamoto E, Griffin J. Analgesics for Osteoarthritis: An Update of the 2006 Comparative Effectiveness Review [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); Available from: <http://www.ncbi.nlm.nih.gov/books/NBK65646/> (accessed on 24 November 2017)
6. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, *et al.* American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res.* 2012 ;64:465–74.
7. Anandacoomarasamy A, March L. Current evidence for osteoarthritis treatments. *Ther Adv Musculoskelet Dis.* 2010;2:17-28.
8. Craig W, Edeer D. Glucosamine and chondroitin sulphate for osteoarthritis. *WorkSafe BC Evidence Based Practice Group;* June 2013.
9. Nicolas P, Tod M, Padoin C, Petitjean O. Clinical pharmacokinetics of diacerein. *Clin Pharmacokinet.* 1998 ;35:347–59.
10. Annual nutrition industry overview. *Nutrition Business J.* 2005;10:6–7.
11. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis. *Ann Rheum Dis.* 1957;16:494–502.
12. Bellamy N, Buchanan WW, Goldsmith CH. Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to anti-rheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol.* 1988;15:1833–40.
13. Uebelhart D. Clinical review of chondroitin sulphate in osteoarthritis. *Osteoarthr Cartil OARS Osteoarthr Res Soc.* 2008;16 Suppl 3:S19–21.
14. Clegg DO, Reda DJ, Harris CL, Klein MA, O'Dell JR, Hooper MM, *et al.* Glucosamine, chondroitin sulphate, and the two in combination for painful knee osteoarthritis. *N Engl J Med.* 2006 23;354:795–808.
15. Singh K, Sharma R, Rai J. Diacerein as adjuvant to diclofenac sodium in osteoarthritis knee. *Int J Rheum Dis.* 2012 ;15:69–77.
16. Burkhard F Leeb. Clinical Efficacy and Safety of Diacerein in Osteoarthritis – A Review. *Eur Musculoskelet Rev.* 2010;5:23–9
17. The Cochrane Collaboration, editor. *Cochrane Database of Systematic Reviews: Reviews* [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 1996. Available from: <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0013261/> (accessed on 24 November 2017)
18. Wandel S, Juni P, Tendal B, Nuesch E, Villiger PM, Welton NJ, *et al.* Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ.* 2010;341(2):c4675.