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A COMPARATIVE STUDY OF CLINICAL EFFICACY AND SAFETY OF GLUCOSAMINE PLUS CHONDROITIN SULPHATE VERSUS NSAIDS IN PATIENTS SUFFERING FROM OSTEOARTHRITIS

Dr. Balla Krishna Sowmya[1*], Dheeraj Neerati[2], Harshitha Nookala[2], G V Sumakavya[3], Dr. Sujith Kumar Vakati[4]

[1*]Assistant Professor, Department of Pharmacology, Mamata Academy of Medical Sciences, Bachupally, Telangana, India
[2]Medical Intern, Mamata Academy of Medical Sciences, Bachupally, Telangana, India
[3]Phase III MBBS student, Mamata Academy of Medical Sciences, Bachupally, Telangana, India
[4]Professor, Department of Orthopaedics, Mamata Academy of Medical Sciences, Bachupally, Telangana, India

***Corresponding Author:** Dr. Balla Krishna Sowmya
*Assistant Professor, Department of *Pharmacology, Mamata Academy of Medical Sciences, Bachupally, Telangana, India, E-mail: bksowmya1987@gmail.com

Abstract

Introduction: Osteoarthritis (OA) is a chronic degenerative joint disease in elderly with higher incidence (22-39%) in India. Despite data from previous studies the prescription of glucosamine plus chondroitin sulphate (GCS) in real-time clinical practice remains meagre. Hence, this study is conducted with the following objectives

Objectives: (1) To evaluate the efficacy of GCS and (2) To compare the efficacy and safety of GCS and NSAIDS in OA.

Materials and Methodology: This was a prospective observational study conducted among OA patients in a tertiary care teaching hospital during July 1st - October 31st 2024 after approval from Institutional Ethics Committee.

Results: Majority of the subjects were females (53.66%). By the end of the study, the mean (SD) total WOMAC score of GCS group was significantly reduced to 23.24 (14.35) with a mean difference (SE) of 13.71 (7.08) and to 18.8 (9.81) with a mean difference (SE) of 20.05 (8.52) in NSAIDs group. The mean difference (SE) of mean change (SD) WOMAC total score and sub scale score for physical function were statistically significant (p = 0.0006) between the study groups. Most common adverse effect among GCS users was abdominal bloating with flatulence while in NSAIDs users was gastro-oesophageal reflux and heart burn. **CONCLUSION:** This study shows the pragmatic evidence on clinical efficacy of GCS in OA of knee with maximal benefit by around 8 weeks. Though not suitable for acute OA knee but may serve as an effective alternative to NSAIDs for long-term management.

Keywords: Osteoarthritis; Glucosamine chondroitin sulphate; WOMAC Scores

Introduction

Osteoarthritis (OA) is a chronic degenerative joint disease which is observed all over the world in the elder set of population with women being at higher risk. India has higher incidence (22-39%) of knee osteoarthritis than the western countries [1].

This devitalising disease leads to structural disability of the joint due to an imbalance between the cartilage that is being worn down and the chondrocytes that are being repaired [2]. OA patients present with joint pain, stiffness and reduced range of movements mostly affecting the knee and hip joints.

The treatment of OA is more of palliative management including physical, pharmacological and surgical approaches [3,4]. Pharmacological interventions available for treatment of OA mainly includes NSAIDS and SYSADOA (Slowly Acting Drugs for OA). Though NSAIDS play a crucial role in pain relief, their gastrointestinal, cardiovascular and renal complications are a major drawback in their prolonged use [5]. Chondroitin sulphate (CS), a natural polymer present in hyaline cartilage and bones, acts as a lubricant and aids in resisting the compression [6]. Data from previous studies suggest that CS showed better pain relief and also a decrease of synovitis by nearly 50% owing to their anti-inflammatory effects [7]. In addition, CS is reported to be safe for use and has minimal to no side effects hence has better GI tolerance compared to NSAIDS [8].

Despite of essential characteristics, CS is still not widely used for the treatment of OA. Though the effectiveness of glucosamine and chondroitin sulphate has been demonstrated by various randomised controlled trials, only a few high-quality trials exist. Moreover, their effectiveness in real-time clinical practice remains meagre. Hence, this study aims to address some of these lacunae in the knowledge of use of chondroitin sulphate and is conducted with the following objectives: (1) To evaluate the efficacy of glucosamine plus chondroitin sulphate and (2) To compare the efficacy and safety of CS and NSAIDS used in the treatment of OA.

Materials and Methodology

This was a prospective observational study conducted among patients diagnosed with OA in the Out Patient Department (OPD) of Department of Orthopaedics in a tertiary care teaching hospital between July 1st 2024 and October 31st 2024. Institutional Ethics Committee approval was obtained before the commencement of the study. Prior to data collection, the study subjects were explained clearly regarding the purpose of study and consent was obtained.

Inclusion Criteria: All patients who

1. Are diagnosed with OA of Knee
2. Are aged ≥ 35 years
3. Have no h/o of trauma to the affected joint and
4. Are willing to provide informed consent are included in the study.

Exclusion Criteria: All patients who

1. Have active / h/o peptic ulcer
2. Have h/o any known food and drug allergies
3. Cannot commute to hospital for review visits
4. Are not willing to provide informed consent are excluded from the study.

Firstly, patients attending the orthopaedic OPD were screened for eligibility. Eligible patients who were prescribed glucosamine plus chondroitin sulphate (GCS) tablets (1500mg per oral once daily) were denoted as Group A and those prescribed NSAIDS (Diclofenac 100mg per oral once/twice daily) by the treating orthopedician were denoted as Group B and enrolled into the study. The data was collected as per the study proforma and entered into Microsoft excel spreadsheet. The study proforma includes the demographic details of the study participants along with their chief complaints, medications prescribed and the pain scores etc. The efficacy of the treatments

prescribed were measured by assessing the symptomatic relief from pain & stiffness and overall improvement in physical functional capacity graded by the scores for pain, stiffness and physical function noted by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at the Baseline and 3 follow-up visits every month. Data on adverse effects were noted and addressed as reported / at the subsequent follow-up visit.

Statistical Analysis

Statistical analysis of the data obtained was done by using Microsoft Excel, Social Science Statistics Calculators and Medcalc. Descriptive statistics were applied to generate percentages and continuous data were summarized as mean ± standard deviation (SD). ANOVA and student t-test and Chi square test of significance were applied as applicable with statistical significance at 95% C.I. and $P < 0.05$.

Results

A total of 55 patients fulfilled the eligibility criteria and were enrolled into study. However, 8 and 3 subjects were lost to follow up at first and second review respectively. By the time of second review, 3 participants had to be excluded from the study due to protocol violation. Hence, a total of 41 participants completed the study and their data was analysed.

At the baseline, the mean age (SD) of participants in group A was 51.90 (9.67) years and group B was 48.65 (8.84) years. Majority of the subjects were females (53.66%). The mean body mass index (BMI) (SD) of group A and B participants was 25.21 (3.87) and 26.69 (3.59) respectively. The mean duration (SD) of osteoarthritic symptoms experienced by the participants in group A was 4.71 ± 3.29 years while in group B was 4.55 ± 2.96 years. There was no statistically significant difference in the mean age (SD), mean BMI (SD) and mean duration (SD) of symptoms between the participants of group A and B.

The mean (SD) total WOMAC score was 36.95 (12.7) in group A and 38.85 (15.92) in group B participants. The mean difference of mean total WOMAC score (SD) and sub scale (Pain, Stiffness and Physical function) scores (SD) of group A and B subjects were not statistically significant (p > 0.05) (Table 1).

Mean (SD) WOMAC Scores	Group A (GCS)	Group B (NSAIDs)	Mean Difference (SE)	P – Value
Total	36.95 (12.7)	38.85 (15.92)	1.9 (4.49)	0.67
Pain	7.81 (2.71)	5.85 (3.99)	-1.96 (1.06)	0.07
Stiffness	1.81 (1.08)	1.45 (0.76)	-0.36 (0.29)	0.23
Physical Function	26.38 (10.49)	31.6 (11.97)	5.22 (3.51)	0.15

Table 1. Baseline Mean (SD) WOMAC scores.

By the end of the study, the mean (SD) total WOMAC score of GCS group was reduced to 23.24 (14.35) with a mean difference (SE) of 13.71 (7.08) and to 18.8 (9.81) with a mean difference (SE) of 20.05 (8.52) in NSAIDs group. There was a statistically significant (p <0.0001) mean difference of mean total WOMAC score (SD) and sub scale scores (SD) before and after treatment among the participants who were prescribed GCS (Table 2).

Mean (SD) WOMAC Scores	Baseline	End of study	Mean difference (SE)	P - Value
Total	36.95 (12.7)	23.24 (14.35)	–13.71 (7.08)	**< 0.0001**
Pain	7.81 (2.71)	4.90 (2.9)	–2.91 (1.64)	**< 0.0001**
Stiffness	1.81 (1.08)	0.48 (0.81)	–1.33 (1.2)	**< 0.0001**
Function	26.38 (10.49)	17.86 (11.07)	–8.52 (5.91)	**< 0.0001**

Table 2: Analysis of change in WOMAC scores in group A (GCS) (n = 21).

The mean difference (SE) of the mean change (SD) WOMAC total score and sub scale score for physical function were statistically significant (p = 0.0006) between GCS group and NSAIDs group (Table 3).

WOMAC score	Group A (GCS)	Group B (NSAIDs)	P- Value
Total	13.71 (7.08)	20.05 (8.52)	**0.0132**
Pain	2.91 (1.64)	2.6 (1.43)	0.5235
Stiffness	1.3 (1.2)	1.3 (0.57)	1.000
Physical Function	8.52 (5.91)	16.2 (7.23)	**0.0006**

Table 3: Comparison of Change in WOMAC scores (Baseline to End of treatment).

The mean difference (SE) of the WOMAC total scores was statistically significant in participants who used GCS in every successive review. However, statistically significant mean difference (SE) of the WOMAC sub scale scores were observed until the 1st follow up visit except for physical function which showed significant mean difference (SE) till the end of the study. Whereas, the mean difference (SE) of the WOMAC total scores and sub scale scores were statistically significant in participants who used NSAIDs only until first 4 weeks (Table 4).

	Group A (GCS)		Group B (NSAIDs)	
	Mean difference (SE)	**P- Value**	**Mean difference (SE)**	**P- Value**
WOMAC Total Scores				
Baseline – 1st	6.48 (0.66)	**<0.0001**	16.65 (1.75)	**<0.0001**
1st – 2nd	4.29 (0.85)	**0.0004**	-1.15 (1.30)	1.0000
2nd – 3rd	2.95 (0.73)	**0.0037**	4.55 (1.60)	0.0611
Pain Score				
Baseline – 1st	1.67 (0.17)	**<0.0001**	2.25 (0.24)	**<0.0001**
1st – 2nd	0.71 (0.23)	**0.0338**	-0.10 (0.16)	1.0000
2nd – 3rd	0.52 (0.19)	0.0741	0.45 (0.21)	0.2784
Stiffness Score				
Baseline – 1st	0.86 (0.16)	**0.0002**	1.10 (0.16)	**<0.0001**
1st – 2nd	0.33 (0.13)	0.0931	0.05 (0.88)	1.0000
2nd – 3rd	0.14 (0.16)	1.0000	0.15 (0.08)	0.4969
Physical Function Score				
Baseline – 1st	3.0 (0.92)	**0.0231**	13.35 (1.52)	**<0.0001**
1st – 2nd	3.24 (0.60)	**0.0002**	-1.65 (1.44)	1.0000
2nd – 3rd	2.29 (0.46)	**0.0004**	4.50 (1.62)	0.0710

Table 4: Analysis of change in WOMAC scores at each review. (1st, 2nd, 3rd indicates respective Reviews).

There was a decreasing trend in consumption of medicines prescribed from 1st first review to the end of the study with a mean (SD) consumption of 78.95 (4.48) pills. As a whole, 95% of the study subjects had more than 80% adherence to the prescribed medications. Most common adverse effect among those who used GCS was abdominal bloating with flatulence followed by gastro-oesophageal reflux, constipation and diarrhoea while in those who used NSAIDs gastro-oesophageal reflux and heart burn were most reported.

Discussion

In this study, altogether 41 patients suffering from OA are divided into group A (GCS) and group B with 21 and 20 participants respectively. A little more than one half of the study participants are females. At the beginning of the study, there is no statistically significant difference between these groups in terms of age, BMI and duration of time they experienced symptoms of osteoarthritis. And also, there is no statistically significant difference in the mean total WOMAC score and sub scale scores.

On completion of the study, it is observed that the mean total WOMAC scores and the sub scale scores of both the groups reduced significantly from the baseline scores. However, the mean change of total WOMAC score and sub scale score for physical function are statistically significant in GCS group when compared to NSAIDs group. The participants on GCS exhibited a statistically significant change in the mean total WOMAC scores and mean sub scale score for physical function

in every review visit. Whereas, statistically significant change in mean scores is observed only in the first 4 weeks in those who are on NSAIDs.

On the whole, almost all of the study participants consumed four-fifths of the medicines prescribed and with time showed a decreasing trend in consumption of medicines prescribed. Medications which may be explained by lesser felt need to take medication following relief of symptoms. Participants who are on GCS complained of abdominal bloating with flatulence and those on NSAIDs had gastro-oesophageal reflux and heart burn.

The mean age participants in this study ranged from 48 – 52 years which is similar to the age distribution observed in other studies on glucosamine (48 – 65 years) conducted in different countries [9-13]. This reinforces the fact that osteoarthritis of knee is an age-related condition with higher prevalence rates with increasing age. This study shows higher prevalence of osteoarthritis in females and similar observation is reported from the study done by Selvan et al. [11]. The BMI of present study subjects falls into overweight category as per WHO and implies that osteoarthritis of knee is associated with increased weight which is in conformity with findings of other studies [11-13].

The baseline WOMAC scores of participants in this study indicate that the subject distribution into two groups is even and comparable in terms of symptom quantification at baseline. There is a highly significant difference in all the scores between baseline and end of study (after 12 weeks) in both the treatment groups ($p < 0001$). This decrease in WOMAC scores in GCS group is similar to those observed in studies done by Giordano N et al. [9] and Selvan et al. [11]. These observations signify the efficacy of glucosamine and chondroitin sulphate in symptomatic improvement of osteoarthritis of knee. Mean WOMAC scores at the end of treatment in both the groups showed no significant difference ($p > 0.05$). This observation suggests that the efficacy of glucosamine and chondroitin sulphate is comparable to NSAIDs which are prescribed routinely in osteoarthritis. However, when mean reductions in each score are compared between the groups GCS are more efficacious in improving overall WOMAC total scores ($p =0.001$) and WOMAC physical function scores ($p=0.0006$).

The change in WOMAC total scores at every successive review was significant in GCS group while a similar pattern was not observed in NSAIDs group. This can be explained based on the fact that NSAIDs tend to cause their effect faster and near maximum effect is attained in a shorter period. This correlates with findings of another trial comparing glucosamine with ibuprofen in osteoarthritis of knee which concluded that there was a time lag for peak glucosamine action while ibuprofen effects were faster [14].

The pain relief with glucosamine is gradual and maximal during first 8 weeks and with subsequent continued treatment, the incremental pain relief is minimal. In NSAIDs group, rapid response was observed by first review (4 weeks) and subsequent reviews showed only marginal, statistically not significant improvements. These results are in concordance with other studies [14,15] on glucosamine which suggested that, unlike NSAIDs, glucosamine is not suitable for treatment of acute symptoms of osteoarthritis but is appropriate for long term management of osteoarthritis, producing global clinical improvements.

Stiffness experienced at baseline was significantly reduced at the first review and thereafter, the change was minimal and insignificant at successive reviews in both the groups. This suggests that GCS and NSAIDs are comparable in relieving stiffness at knee joint associated with osteoarthritis.

There is a gradual and more or less uniform improvement in function scores in GCS group at every successive review starting from baseline; whereas, in NSAIDs group, although there was significant improvement at every review compared to baseline, the change was not uniform at every successive review. The magnitude of change in function scores from baseline to first review (4 weeks) was more than double in NSAIDs group compared to GCS group which suggests the faster rates of recovery of function with NSAIDs and slow, sustained and uniform rate of recovery in glucosamine group.

Conclusion

This study has put forth the pragmatic evidence on clinical efficacy of glucosamine and chondroitin sulphate in treatment of osteoarthritis of knee. Maximal benefit with GCS is seen by around 8 weeks with marginal incremental benefits on continued use. GCS, as a single agent, is not suitable for treatment of acute symptoms of OA of knee; it may serve as adjunct/an effective alternative to NSAIDs for long term management of osteoarthritis of knee.

Conflicts of Interest: Nil.

References

1. Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology of knee osteoarthritis in India and related factors. Indian J Orthop. 2016 Sep;50(5):518-522 Doi:10.4103/0019-5413.189608. PMID: 27746495; PMCID: PMC5017174.
2. Man GS, Mologhianu G. Osteoarthritis pathogenesis – a complex process that involves the entire joint. J Med Life. 2014 Mar 15;7(1):37-41. Epub 2014 Mar 25 PMID: 24653755; PMCID: PMC3956093.
3. Reginster JY, Veronese N. Highly purified chondroitin sulfate: a literature review on clinical efficacy and pharmacoeconomic aspects in osteoarthritis treatment. Aging Clin Exp Res. 2021 Jan;33(1):37-47. Doi: 10.1007/s40520-020-01643-8. Epub 2020 Jul 7. PMID: 32638342; PMCID: PMC7897612.
4. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis Care Res (Hoboken). 2020 Feb;72(2):149-162. Doi: 10.1002/acr.24131. Epub 2020 Jan 6. Erratum in: Arthritis Care Res (Hoboken). 2021 May;73(5):764. Doi: 10.1002/acr.24615. PMID: 31908149.
5. Bindu S, Mazumder S, Bandyopadhyay U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. Biochem Pharmacol. 2020 Oct; 180:114147. Doi: 10.1016/j.bcp.2020.114147. Epub 2020 Jul 10. PMID: 32653589; PMCID: PMC7347500.
6. Pal D, Saha S. Chondroitin: a natural biomarker with immense biomedical applications. RSC Adv. 2019 Sep 6;9(48):28061-28077. Doi: 10.1039/c9ra05546k. PMID: 35530463; PMCID: PMC9071010.
7. Tío L, Orellana C, Pérez-García S, Piqueras L, Escudero P, et al. Effect of chondroitin sulphate on synovitis of knee osteoarthritic patients. Med Clin (Barc). 2017 Jul 7;149(1):9-16. English, Spanish. Doi: 10.1016/j.medcli.2016.12.045. Epub 2017 Feb 27. PMID: 28245911.
8. Reginster JY, Veronese N. Highly purified chondroitin sulfate: a literature review on clinical efficacy and pharmacoeconomic aspects in osteoarthritis treatment. Aging Clin Exp Res. 2021 Jan;33(1):37-47. Doi: 10.1007/s40520-020-01643-8. Epub 2020 Jul 7. PMID: 32638342; PMCID: PMC7897612.
9. Giordano N, Fioravanti A, Papakostas P, Montella A, Giorgi G, et al. The efficacy and tolerability of glucosamine sulfate in the treatment of knee osteoarthritis: A randomized, double-blind, placebo-controlled trial. Current Therapeutic Research. 2009;70(3):185-196
10. Clegg D, Reda D, Harris C, Klein M, O'Dell J, et al. Glucosamine, Chondroitin Sulfate, and the Two in Combination for Painful Knee Osteoarthritis. New England Journal of Medicine. 2006;354(8):795-808.
11. Selvan T, Rajiah K, Nainar M, Mathew E. A Clinical Study on Glucosamine Sulfate versus Combination of Glucosamine Sulfate and NSAIDs in Mild to Moderate Knee Osteoarthritis. The Scientific World Journal. 2012;2012:1-5.
12. Petersen S, Saxne T, Heinegard D, Hansen M, Holm L, et al. Glucosamine but not ibuprofen alters cartilage turnover in osteoarthritis patients in response to physical training. Osteoarthritis and Cartilage. 2010;18(1):34-40.

13. Cibere J, Kopec J, Thorne A, Singer J, Canvin J, et al. Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. Arthritis & Rheumatism. 2004;51(5):738-745.
14. Mullerfasbender H, Bach G, Haase W, Rovati L, Setnikar I. Glucosamine sulfate compared to ibuprofen in osteoarthritis of the knee. Osteoarthritis and Cartilage. 1994;2(1):61-69.
15. Noack W, Fischer M, Forster K, Rovati L, Setnikar I. Glucosamine sulfate in osteoarthritis of the knee. Osteoarthritis and Cartilage. 1994;2(1):51-59.