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Original Research Article

Comparison of efficacy of glucosamine, chondroitin sulfate and a fixed dose combination of glucosamine and chondroitin sulfate in the treatment of osteoarthritis

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ABSTRACT

Background: The study aimed to compare the efficacy of glucosamine, chondroitin sulfate and a fixed dose combination (FDC) of glucosamine and chondroitin sulfate in patients with osteoarthritis (OA) of the knee.
Methods: This was an open-label prospective comparative cohort study conducted from November 2023 to April 2024. Subjects were recruited consecutively from the orthopaedics outpatient department of GCMCH, Chidambaram, and assigned to one of three treatment groups based on the treating physician's prescription. Study tools including a patient data collection form and Western Ontario McMaster Universities Arthritis Index (WOMAC) questionnaires were used to measure outcomes at baseline and at monthly intervals over 4 months.
Results: After 4 months, the fixed dose combination group showed a statistically significant reduction in WOMAC pain score compared to glucosamine and chondroitin sulfate monotherapy groups (p=0.009). No significant differences were observed among the groups for stiffness (p=0.234) or physical function (p=0.439). The fixed dose combination consistently produced the greatest numerical improvement across all WOMAC domains.
Conclusions: The fixed dose combination of glucosamine 750 mg and chondroitin sulfate 600 mg is slightly more effective than either agent used alone, demonstrating greater relief of pain in patients with osteoarthritis of the knee.

Keywords: Chondroitin sulfate, Glucosamine, Osteoarthritis, Pain, Physical function, Stiffness, WOMAC

INTRODUCTION

Osteoarthritis (OA) is among the most prevalent forms of arthritis, representing a chronic, degenerative, and disabling condition marked by intricate disruptions across the entire synovial joint. These include structural impairments in hyaline articular cartilage, compromised subchondral bone integrity, tissue hypertrophy, increased vascularity within the synovium, and instability affecting tendons and ligaments.[1]

As degeneration progresses, irreversible damage occurs in the articular cartilage and other joint structures. Despite being the most widespread musculoskeletal disorder globally, extensive research has yet to pinpoint its precise cause. The pain associated with OA originates in the bone and surrounding joint structures, with crystals and intra-articular swelling serving as significant contributors to discomfort. OA commonly affects the proximal and distal interphalangeal joints of the hands, the first carpometacarpal joint of the thumb, as well as the knees, hips, and the lumbar and cervical spine. In India, OA affecting the knees and spine is particularly prevalent,

while OA of the hip remains relatively rare.[2] Risk factors are generally categorised into non-modifiable elements (such as age, gender, and genetics) and modifiable ones (including obesity, dietary habits, and mechanical stress), some of which may help reduce the likelihood of developing OA.[3]

Symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) exhibit structure-modifying properties due to their ability to stimulate anabolic activity in the cartilage matrix, inhibit lysosomal enzyme function, and enhance chondrocyte activity. In terms of structural improvement, standalone treatments using glucosamine (GA) and chondroitin sulfate (CS) have demonstrated a statistically meaningful decrease in joint space narrowing.[4]

The purpose of this study was to compare the efficacy of glucosamine, chondroitin sulfate and a fixed dose combination of glucosamine and chondroitin sulfate in patients with osteoarthritis of the knee.

METHODS

Study design

This open-label prospective comparative cohort study was conducted from November 2023 to April 2024 at the Government Cuddalore Medical College Hospital (GCMCH), Chidambaram. Subjects were recruited consecutively from the orthopaedics outpatient department following a clinical diagnosis of mild or moderate osteoarthritis of the knee. In total, 60 patients were interviewed, of whom 45 met the eligibility criteria and were enrolled into the study. Of these, 15 subjects dropped out due to loss to follow-up or refusal to continue therapy, and 30 subjects completed the study.

Subjects were assigned to one of three treatment groups based on the treating physician's prescription: Group 1 (n=10) received glucosamine 750 mg; Group 2 (n=10) received chondroitin sulfate 600 mg; and Group 3 (n=10) received a fixed dose combination of glucosamine 750 mg and chondroitin sulfate 600 mg. All subjects received their respective medications immediately after enrolment. Clinical assessments were scheduled at baseline (Visit 1-V1), 30 days (Visit 2-V2), 60 days (Visit 3-V3), 90 days (Visit 4-V4), and 120 days (Visit 5-V5).

Inclusion criteria

Patients aged above 40 years of either gender diagnosed with osteoarthritis of the knee, patients with diabetes and cardiovascular risk were included in the study, newly diagnosed osteoarthritis patients, and all subjects provided written informed consent prior to enrolment in the study were included.

Exclusion criteria

Diagnosis of other diseases of the knee, patients who were not willing to participate, and any condition that, in the investigator's opinion, made the subject unfit for the study were excluded.

Outcome measures

The Western Ontario McMaster Universities Arthritis Index (WOMAC) osteoarthritis index is a disease-specific, self-administered health status measure that is widely accepted as reflective of osteoarthritis disease activity. The original index consists of 24 questions (5 pain, 2 stiffness, and 17 physical function). Individual question responses are assigned a score between 0 (none) and 4 (extreme) and summed to form a score ranging from 0 (best) to 96 (worst). There are three sections: Section A addresses the amount of pain (5 questions), Section B addresses the amount of joint stiffness (2 questions), and Section C addresses aspects of physical function (17 questions).[5]

Statistical analysis

Baseline demographic information including age, sex, comorbidities, and medication history was collected from the patient's case sheet and direct interview. Study tools such as a patient data collection form and Western Ontario McMaster Universities Arthritis Index (WOMAC) osteoarthritis questionnaires were used.[5] Documented data were entered into JASP (Jeffreys's Amazing Statistics Program) and a one-way analysis of variance (ANOVA) was performed to determine whether there was a statistically significant difference in mean WOMAC scores between the three treatment groups. Post hoc comparisons were conducted using the Tukey HSD test. Statistical significance was set at $p<0.05$.

Ethical considerations

The study was started after receiving official approval from the ethics committee of GCMCH, Chidambaram. Ethical approval was necessary to protect the rights of the participants. Written informed consent, participant safety, and confidentiality were strictly maintained throughout the study. Every participant provided written informed consent before enrolment and participation in the study.

RESULTS

Baseline demographic and clinical characteristics of all three groups are presented in Table 1. In total, 60 patients were interviewed. Of these, 45 subjects with OA of the knee met the inclusion criteria and were enrolled, and divided into three groups of 10. Fifteen subjects dropped out of the study because they were lost to follow-up or refused further therapy. Finally, 30 subjects completed the study: Group 1 (glucosamine, n=10), Group 2 (chondroitin sulfate, n=10), and Group 3 (fixed dose combination of glucosamine and chondroitin sulfate, n=10). All subjects received medication immediately after enrolment.

Among the study population, the percentage of female subjects (76.7%) was greater than male subjects (23.3%)

across all three groups, indicating that females are more prone to osteoarthritis. Subjects within the age group of 40–49 years numbered 10 (33.3%), and those aged 50-59 years numbered 13 (43.3%). Among all subjects, 19 (63%) belonged to the occupation group of daily wage workers, compared to homemakers and subjects unable to walk, suggesting that daily wage workers were most affected by osteoarthritis.

Table 1: Baseline and clinical demographic characteristics of all three treatment groups.

Parameters	GA [n=10]	CS [n=10]	FDC of GA and CS [n=10]
Mean age (years)	59±12.06	56.3±9.47	58.6±6.74
Age (years)			
≥40 to 49, % (N)	20 (2)	20 (2)	30 (3)
50 to 59, % (N)	30 (3)	50 (5)	20 (2)
≥60, % (N)	50 (5)	30 (3)	50 (5)
Male, % (N)	40 (4)	10 (1)	10 (1)
Female, % (N)	60 (6)	90 (9)	90 (9)
Height (cm)	168.9±3.3	168.8±5.11	169.3±6
Weight (kg)	75.3±6.48	73.2±5.84	75.5±4.20
BMI (kg/m^2)	26.53±2.88	25.79±2.93	26.49±2.95
WOMAC score			
Pain	19.5±0.67	19.7±0.46	19.7±0.46
Stiffness	8	8	7.8±0.4
Physical function	63.2±2.27	63.9±2.21	63.9±5.13

The mean body mass index (BMI) of all subjects was assessed. Among them, the percentage of subjects in the BMI group of 18.5-24.9 (normal weight) was 47% (n=14), 25-29.9 (overweight) was 30% (n=9), and >30 (obese) was 23% (n=7). Although the majority of subjects fell within the normal weight range, a combined 53% were overweight or obese (BMI ≥25), suggesting that excess body weight may contribute to the development of osteoarthritis, which is consistent with established risk factors.

WOMAC pain

The mean and standard deviation for WOMAC pain scores at the end of the study (4th month) were as follows: Group 1 (GA): M=19.44±0.144; Group 2 (CS): M=19.6±0.1; Group 3 (FDC): M=16.96±2.1385. The results of the ANOVA indicated that there was a statistically significant difference in WOMAC pain score between the groups, F(2,12)=7.15077, p=0.00902.

Post hoc comparison using the Tukey HSD test revealed that Group 1 was not statistically different from Group 2 (p=0.97728). However, Group 3 was statistically significantly different from both Group 1 (p=0.02051) and Group 2 (p=0.01421). These results indicate that Group 3 demonstrated a statistically significantly lower WOMAC pain score compared to Groups 1 and 2, reflecting superior pain relief with the fixed dose combination. There was no significant difference between Group 1 and Group 2, indicating similar efficacy of glucosamine and chondroitin sulfate monotherapy in pain management.

WOMAC stiffness

The mean and standard deviation for WOMAC stiffness scores at the end of the study were as follows: Group 1 (GA): M=7.32±0.4764; Group 2 (CS): M=6.5±0.9083; Group 3 (FDC): M=6.76±0.7403. The results of the ANOVA indicated that there was no statistically significant difference in WOMAC stiffness score between the groups, F(2,12)=1.64625, p=0.2335.

Post hoc comparison using the Tukey HSD test revealed that Group 1 was not statistically different from Group 2 (p=0.21909), Group 1 was not statistically different from Group 3 (p=0.46862), and Group 2 was not statistically different from Group 3 (p=0.84191). These results indicate that there was no statistically significant difference in stiffness scores among Groups 1, 2, and 3. All three treatments produced comparable and modest reductions in joint stiffness over the 4-month period.

WOMAC physical function

The mean and standard deviation for WOMAC physical function scores at the end of the study were as follows: Group 1 (GA): M=59.82±2.8908; Group 2 (CS): M=57.68±5.2179; Group 3 (FDC): M=55.92±5.4048. The results of the ANOVA indicated that there was no statistically significant difference in WOMAC physical function score between the groups, F(2,12)=0.88305, p=0.4388.

Post hoc comparison using the Tukey HSD test revealed that Group 1 was not statistically different from Group 2 (p=0.75201), Group 1 was not statistically different from Group 3 (p=0.40794), and Group 2 was not statistically different from Group 3 (p=0.82339). These results indicate that there was no statistically significant difference in physical function scores between Groups 1, 2, and 3. The longitudinal changes in all three WOMAC subscales across all five study visits are presented in Table 2.

WOMAC total score

The mean and standard deviation for total WOMAC scores at the end of the study were as follows: Group 1 (GA): M=85.32±3.5003; Group 2 (CS): M=81.86±5.713; Group 3 (FDC): M=78.98±7.5843. The results of the ANOVA indicated that there was no statistically significant difference in total WOMAC score between the groups, F(2,12)=1.47594, p=0.2672.

Post hoc comparison using the Tukey HSD test revealed that Group 1 was not statistically different from Group 2 (p=0.62877), Group 1 was not statistically different from Group 3 (p=0.23946), and Group 2 was not statistically different from Group 3 (p=0.72221). Although no statistically significant difference was found for the total WOMAC score, Group 3 consistently showed the lowest (most favourable) total scores across all visits, and the numerical trend favours the fixed dose combination in overall OA management.

Table 2: Changes in mean WOMAC scores across the five study visits (mean±SD).

Group	Subscale	Baseline (V1)	1st month (V2)	2nd month (V3)	3rd month (V4)	4th month (V5)
GA	Pain	19.5±0.67	19.6±0.66	19.4±0.8	19.4±0.66	19.3±0.78
	Stiffness	8	7.6±0.66	7.2±0.98	6.9±0.94	6.9±0.94
	Physical function	63.2±2.27	61.9±2.54	60.1±3.88	57.7±4.47	56.2±4.55
CS	Pain	19.7±0.46	19.7±0.46	19.6±0.5	19.5±0.5	19.5±0.5
	Stiffness	8	6.7±0.9	6.1±1.13	5.9±1.3	5.8±1.25
	Physical function	63.9±2.21	61.6±2.54	57.8±2.89	53.6±3.35	51.5±4.78
FDC of GA and CS	Pain	19.7±0.46	18.4±1.2	16.8±1.4	15.5±1.43	14.4±1.62
	Stiffness	7.8±0.4	7.2±0.87	6.6±1.2	6.2 ± 1.4	6.0±1.34
	Physical function	63.9±5.13	58.9±2.21	53.8±2.89	52.1±2.91	45.6±2.24

Table 3: One-way ANOVA statistical analysis of WOMAC scores across all three treatment groups.

WOMAC score	ANOVA	SS	df	MS	F value	Significance
Pain	Between-treatment	21.9	2	10.955	7.150	0.009021*
	Within-treatment	18.384	12	1.532		
	Total	40.293	14			
Stiffness	Between-treatment	1.756	2	0.878	1.646	0.2335
	Within-treatment	6.4	12	0.5333		
	Total	8.156	14			
Physical function	Between-treatment	38.145	2	19.073	0.883	0.4388
	Within-treatment	259.18	12	21.599		
	Total	297.329	14			
Total	Between-treatment	100.769	2	50.385	1.475	0.2672
	Within-treatment	409.648	12	34.137		
	Total	510.417	14			

*p<0.05 indicates statistical significance; SS = Sum of Squares; df = degrees of freedom; MS = Mean Square

Outcomes

The primary outcome measure was the change in WOMAC pain, stiffness, and physical function scores from baseline to the end of 4 months of treatment across the three groups. The full statistical summary is presented in Table 3.

Pain (WOMAC Section A): The fixed dose combination group (Group 3) demonstrated the most clinically meaningful reduction in pain score, declining from a baseline of 19.7±0.46 to 14.4±1.62 at 4 months a reduction of approximately 5.3 points. In contrast, the glucosamine group (Group 1) showed only a marginal decrease from 19.5±0.67 to 19.3±0.78, and the chondroitin sulfate group (Group 2) showed virtually no change, declining from 19.7±0.46 to 19.5±0.50. The ANOVA revealed a statistically significant difference in WOMAC pain scores among the three groups [F(2,12)=7.150, p=0.009]. Post hoc analysis (Tukey HSD) confirmed that Group 3 was significantly different from both Group 1 (p=0.021) and Group 2 (p=0.014), while Groups 1 and 2 did not differ significantly from each other (p=0.977). These findings indicate that the fixed dose combination was superior to either monotherapy in relieving pain.

Stiffness (WOMAC Section B): All three groups showed a gradual reduction in stiffness scores over the 4-month period. Group 1 declined from 8.0 to 6.9±0.94; Group 2 showed a reduction from 8.0 to 5.8±1.25; and Group 3 declined from 7.8±0.4 to 6.0±1.34. However, the ANOVA did not reveal a statistically significant difference among the groups [F(2,12)=1.646, p=0.234], and post hoc analysis confirmed no significant pairwise differences (Group 1 vs. 2: p=0.219; Group 1 vs. 3: p=0.469; Group 2 vs. 3: p=0.842). This suggests that all three treatments had comparable and modest effects on joint stiffness.

Physical Function (WOMAC Section C): All three groups showed progressive improvement in physical function over 4 months. Group 1 improved from 63.2±2.27 to 56.2±4.55; Group 2 improved from 63.9±2.21 to

51.5±4.78; and Group 3 showed the greatest improvement, declining from 63.9±5.13 to 45.6±2.24. Despite this trend favouring the FDC group, the ANOVA did not demonstrate a statistically significant difference among the groups [F(2,12)=0.883, p=0.439], and post hoc analysis confirmed no significant pairwise differences (Group 1 vs. 2: p=0.752; Group 1 vs. 3: p=0.408; Group 2 vs. 3: p=0.823). These results suggest a trend toward better functional improvement with the FDC, though it did not reach statistical significance, possibly due to the small sample size.

Total WOMAC Score: The total WOMAC scores at 4 months were Group 1: 85.32±3.50, Group 2: 81.86±5.71, and Group 3: 78.98±7.58. Although Group 3 had the lowest total score (indicating better overall health status), the ANOVA showed no statistically significant difference [F(2,12)=1.476, p=0.267]. The numerical trend, however, consistently favoured the fixed dose combination across all WOMAC domains.

Summary of outcomes

Across the 4-month study period, the fixed dose combination of glucosamine 750 mg and chondroitin sulfate 600 mg demonstrated statistically significant superiority over monotherapy specifically in the domain of pain relief (p=0.009). For joint stiffness (p=0.234), physical function (p = 0.439), and total WOMAC score (p=0.267), no statistically significant differences were observed among the groups, though the FDC consistently showed the greatest numerical improvement. No adverse events were reported in any treatment group throughout the study.

DISCUSSION

A meta-analysis of randomized controlled trials on the effectiveness and safety of glucosamine and chondroitin for the treatment of osteoarthritis has shown that these agents are believed to have potential benefits in reducing pain, improving joint function, and slowing the progression of joint damage. However, the effectiveness of these agents remains a subject of debate, and more research is needed to establish their overall efficacy. Significant benefits associated with the use of glucosamine or chondroitin sulfate alone have not been consistently identified across all studies.[10] A systematic review and meta-analysis on the efficacy and safety of the combination of glucosamine and chondroitin for knee osteoarthritis concluded that the combination group showed a statistically significant advantage over monotherapy groups, while individual agents showed no significance in several outcomes. The present study supports these findings, as the combination group demonstrated statistical significance for WOMAC pain score compared to monotherapy.[11]

Our findings support the efficacy and safety of the fixed dose combination of glucosamine and chondroitin sulfate. However, there remains much discussion in the scientific literature regarding the role of this combination in knee OA, owing to controversial results from previous clinical studies. In a combined treatment trial with chondroitin sulfate and glucosamine sulfate, the combination was not observed to be superior to placebo during a 6-month treatment period.[12]

A systematic review and meta-analysis evaluating the efficacy and safety of glucosamine sulfate, chondroitin sulfate, and their combination regimen in the management of knee osteoarthritis showed that chondroitin sulfate reduced pain intensity and improved physical function, while glucosamine sulfate showed reduction in joint space narrowing. The combination regimen in that analysis showed no reduction in pain intensity or improvement in physical function. In contrast, the present study concludes that the combination regimen reduced pain intensity more effectively than glucosamine or chondroitin sulfate administered alone.[13]

The present study is limited by its small sample size of 30 subjects, which can significantly impact the generalisability of the findings, making it difficult to confidently apply the results to a larger, more diverse population. The study was also conducted over a relatively short time period, which means that long-term effects developing beyond the 4-month observation window may not have been captured. Furthermore, the absence of a placebo control group is a notable limitation; the observed improvement in WOMAC scores may partly reflect natural fluctuation in OA symptoms or a placebo effect, rather than solely the pharmacological efficacy of the treatments under study. Future studies with larger sample sizes, longer follow-up durations, and placebo-controlled designs are recommended to validate these findings.

CONCLUSION

This study demonstrates the efficacy and safety of glucosamine 750 mg, chondroitin sulfate 600 mg, and a fixed dose combination of glucosamine 750 mg and chondroitin sulfate 600 mg in patients with osteoarthritis, based on comparison of WOMAC pain, stiffness, physical function, and total scores over a period of 4 months. The results revealed that the fixed dose combination of glucosamine 750 mg and chondroitin sulfate 600 mg showed significantly better improvement in pain compared with glucosamine 750 mg or chondroitin sulfate 600 mg alone. In terms of safety, no subjects experienced adverse events in any of the three treatment groups throughout the study duration.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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