



## Original Article

## Effects of Combined Glucosamine/Chondroitin with Structured Physical Therapy Program on Knee Osteoarthritis: A Randomized Control Trail

Muhammad Salman<sup>1</sup>, Aamer Naeem<sup>2</sup>, Muhammad Umar<sup>3</sup>, Somiya Asif<sup>4</sup>, Kiran Haq<sup>5</sup> and Muhammad Saad Hasan<sup>6</sup>

<sup>1</sup>Department of Neurology, Center of Advanced Studies in Health & Technology, Rawalpindi, Pakistan

<sup>2</sup>Department of Rehabilitation Sciences, Foundation University Islamabad, Pakistan

<sup>3</sup>Department of Rehabilitation Sciences, IAHS, Rawalpindi Medical University, Rawalpindi, Pakistan

<sup>4</sup>Department of Physiotherapy, Margalla Institute of Health Sciences, Islamabad, Pakistan

<sup>5</sup>Department of Physiotherapy, Rawal Institute of Health Sciences, Islamabad, Pakistan

<sup>6</sup>Department of Physiotherapy, Rawal Institute of Rehabilitation Sciences Islamabad, Pakistan

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**\*Corresponding Author:**

Muhammad Salman

Department of Neurology, Center of Advanced Studies in Health & Technology, Rawalpindi, Pakistan  
[physiosalmanok@gmail.com](mailto:physiosalmanok@gmail.com)

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## ABSTRACT

Osteoarthritis is the most debilitating condition in general population. The incidence rate of this condition is very high. **Objective:** this study was conducted to observe the effectiveness of glucosamine/chondroitin alone and in combination with physiotherapy on Knee osteoarthritis.

**Methods:** A randomized control trail registered at [clinicaltrials.gov](http://clinicaltrials.gov) under the trail no of NCT05321836. Data was collected from the Physiotherapy clinic and Neurocounsel Hospital Islamabad from 26 July 2021 to 25<sup>th</sup> March 2022. 30 participants met inclusion criteria and were randomly divided into two groups via envelop method. The experimental group was given unlabeled 1500/1200 mg of GH/CS per day for period of 6 months along with physiotherapy treatment for two months (3 sessions per week). The Control group was treated with 1500/1200 mg of unlabeled GH/CS per day for 6 months. Tools used to measure the outcome were WOMAC scale & SF-36. Measure were taken at baseline, 4<sup>th</sup> week and at 8<sup>th</sup> week. Repeated Measure ANOVA was used to analyze results at various weeks and Post Hoc analysis was opted for comparison between groups. SPSS version 21.0 was used for data analysis **Results:** Means±S.D of age in experimental & control group was 64.80±9.65, 60.93±7.61 respectively. Repeated measure ANOVA within both groups significant difference at various weeks of treatment as  $p < 0.05$ . Between groups, Independent t' test also revealed statistically significant difference as  $p$ -value was  $< 0.05$ . **Conclusion:** GH/CS along with physiotherapy is very effective in reducing patient's pain, improving functions, mobility along with quality of life as compared to GH/CS alone.

## INTRODUCTION

Osteoarthritis is the disease of synovial joint which is considered to be the most bothersome arthritic condition among older population. The progressive degeneration of subchondral bone along with synovial membrane starts due to metabolic & structural changes in joints. So, OA is not just the involvement of cartilage but also of synovial membrane and subchondral bone [1]. OA is classified into different phenotypes i.e mechanical induced, OA due to obesity, aging related osteoarthritis etc. stratification of its management related to specific phenotype is thought to be effective in each condition. Identification of specific

phenotype is a challenge for clinicians [2]. SYSADOA (symptomatic slow acting drugs for osteoarthritis) includes two natural substances, one is glucosamine and other is chondroitin sulfate. Some of these compounds have also the ability to modify disease progression (DMOAD) on narrowing of joint space when measurement taken on radiographs [3]. QARSI, in year 2008 published guidelines for the management of Hip and Knee OA along with consensus from some experts in the field that glucosamine sulfate and chondroitin sulfate have the disease modifying capabilities with respect to structural cartilage change.

Treatment should be discontinued if no improvement is observed after 6 months use [4]. Later studies supported these recommendations. In MOVES trail it was observed that 6 months use of fixed dose GS/CS efficacy combination has effects on pain functioning of patients comparable to celecoxib. Both treatments have significant reduction in patient's pain clinically approximately around 50%. Also, neck stiffness (celecoxib 49.2% & 46.9% in GS/CS) and functioning (46.4% & 45.6% respectively) of patient showed comparable outcomes. Euro-5D-5L showed marked improvement in quality of life along with pain reduction on VAS (visual analog scale). OMERACT-QARSI criteria was met by more than eighty percent of patients. Joint effusion and swelling were also improved in both groups [5]. Outcome by the use of glucosamine and Chondroitin sulfate are slow in onset but has long lasting effects on severity of pain reduction and also enhances the patient's quality of life. Patient's physical functional improvement has also been demonstrated. Exercises play a vital role in the management of knee osteoarthritis. Different exercise protocols are done in this regard i.e ROM (range of motion) exercises, strength & endurance training etc. Home plan exercises and education of patient are also crucial. Manual therapists & PT (Physiotherapist) use various exercise programs in combination to improve patient pain and quality of life. Mobilization of joint and soft tissues along with Maitland & Kalternborn joint oscillations traction are first step treatment protocols aim to reduce pain, disability & to improve joint stability along with mobility of OA patients. Knee flexion is the most bothersome mobility disorder of OA sufferer due to joint restricted movement. Many randomized control trials have demonstrated the effectiveness of above-mentioned manual techniques in relieving pain and improving mobility and QoL of osteoarthritis sufferer [6]. There is no consensus in literature on GS/CS along with manual therapy on the management of knee OA. This study will be helpful clinically in the management for OA which will be less expensive and non-invasive as well. The rationale of this study was to compare the effectiveness of glucosamine chondroitin alone & in combination with manual therapy on the management of knee osteoarthritis.

## METHODS

A single blind randomized contrail was registered at clinicaltrials.gov under trail registry number NCT05321836, was conducted in 30 patients at the physiotherapy clinic and the Neurocouncil, Islamabad. Patients were divided into two equal groups by non-probability simple convenient sampling technique. WHO calculator was used for sample size calculation & significant level was set 5% and 95% was power of study. Patient who were more than 50 years of

age. Kellgren grade I-III (radiological evidence of OA who fall in these grades). All those patients who met ACR criteria. Radiographic confirmation of OA by their primary Physician & those not involved in any other study or taking other drugs were all included. And following patients were excluded, those patients who have dementia and having MMSE (mini mental status examination) score less than 24. Any type of cancer except skin cancer. Anemic patients who have Hb level below 10 or HCT <32 and also hemophilic because such patients cannot do adequate exercise due to their low tolerance and hemophilic has the tendency to bleed in their joints as well. Renal insufficiency. Hepatic disorder as glucosamine is metabolized in liver. Those who are unable to walk for 6 minutes and complete 128 m distance in such time interval. Patients who are involved in ant other study or taking other medications for OA. After taking approval from ethical review committee via reference no ERC75/14 participants were divided to either group A (control group) glucosamine plus CS group & group B (experimental group) glucosamine+chondroitin with physiotherapy group. The group A was treated with unlabeled 1500/1200 mg of GH/CS per day for period of six months. The participants were free to choose either once (OD) or TD (three times per day) regimens. The control group was given unlabeled dose of GH/CS 1500/1200 mg per day for six months along with physiotherapy treatment consisting of manual therapy combined with different exercises for a total of 24 sessions spanning across two months (3 sessions per week). Each participant was evaluated by research interventionist to monitor study drug & rescue medication usage (pill counts). The physiotherapy session instigated and ended with warm-up and cool-down period of 5-min, correspondingly. The exercise stage included manual therapy session (two sets of tibifemoral & patellofemoral oscillations) along with 20 min of strength training. Each strength drill session comprised of 10 to 12 repetitions of the subsequent exercises: (1) leg curl, (2) leg extension with heel raise, and (4) step up. Weight was augmented from 2.5 to 5 lb. increments, depending on the patients, after 12 repetitions of two sets had been performed for consecutive two days. A 1 to 1.5 min rest interval separated each exercise. The assessment was carried out using WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) for measuring the health status including pain, stiffness, and function. Quality of life was assessed using SF-36 questionnaire.

## RESULTS

In experimental group the means+S.D of age was 64.80+9.65 where as in control group it was 60.93+7.61. The frequency of male in experimental group was 4(26.7) and of females was 11(73.3). but in control group n=7 (46.7) were

males and n=8(53.3) were females. We employed repeated measure ANOVA to analyze the data at 0th, 4th, 8th week intervals. But for quality of life (SF-36) our data was not normally distributed so test of choice was Man Whitney U test. For WOMAC Scale repeated measure ANOVA showed in experimental group mean+SD at baseline was 0.72+0.16 and at 4th & 8th week was 0.60+0.12 & 0.41+0.20 respectively. The p-value was <0.05 which demonstrated that there was a significant difference at various weeks of treatment in experimental group. In control group the mean+SD at baseline, 4th & 8th week were 0.70+0.12, 0.64+0.12 & 0.51+0.20 respectively. P-value was also <0.05 which also showed improvement in control group. For QoL, we used SF-36 questionnaire, median and interquartile of experimental group at baseline was 37.82(1.75) & in control group it was 36.89(21). But after the intervention when we compared the results in both groups at 8th week in control group the median and IQ was 76.62(3) & in experimental group it was 92.56(3.47). p-value was 0.000\*\*\* which was <0.05. This implied that with the use of physiotherapy along with glucosamine chondroitin had much improvement as compared to control group intervention (Table 1).

Repeated measure ANOVA				
Variable (WOMAC)	Baseline value Mean+SD	4th week value Mean+SD	8th week value Mean+SD	p-value
Experimental group	0.72+0.16	0.60+0.12	0.41+0.20	0.001***
Control group	0.70+0.12	0.64+0.12	0.51+0.20	0.003**
Man-Whitney U test between groups analysis				
	Experimental group Median (IQ)	Control group Median (IQ)	p-value	
SFQOL (0 week)	37.82(1.75)	36.89(21)	0.04	
SFQOL (8 week)	92.56(3.47)	76.62(3)	0.000*	

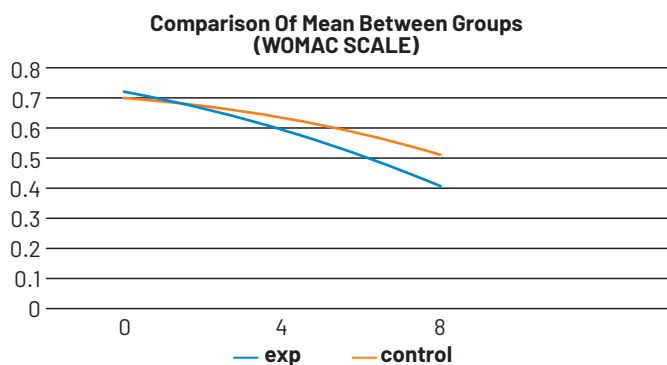
**Table 1:** Between groups Analysis (Statistical Tests)

As our data was normally distributed for WOMAC scale so we used this statistical test. We used Post Hoc analysis for comparison between various week in both groups as mentioned in table 2.

Experimental group	Mean+SD	Mean difference	p-value
0-4	0.60+0.12	0.12	0.004*
4-8	0.41+0.20	0.19	0.001*
0-8	0.41+0.20	0.31	0.000**
Control group			
0-4	0.64+0.12	0.06	0.01*
4-8	0.51+0.20	0.13	0.01*
0-8	0.51+0.20	0.19	0.001**

**Table 2:** Post Hoc Analysis of Variable in both Groups

To compare the mean of WOMAC scale between groups we used independent t' test. It was obvious from the graph that experimental group participants had much improvement in mean score after 4th and 8th week as compared to control group (Figure 1).



**Figure 1:** Independent T' Test for between groups Analysis

## DISCUSSION

Glucosamine in combination with chondroitin sulfate have widely gained population as an alternative treatment for OA. Two studies of long-term duration have demonstrated that patient self-reported pain and physical function has significantly improved after 3 years of treatment with these compounds [7, 8]. Another study also supported abovementioned results by depicting no reduction in joint space after CS administration for 2 years. But no significant improvement was observed relative to placebo [9]. Various studies have confirmed that combination of GS/CS has beneficial effects on knee OA and can be utilized as alternative treatment option [10]. One research has confirmed that glucosamine plus Chondroitin sulfate have significant role in reduction of participants moderate to severe pain intensity in subset analysis. In patient groups significant reduction in mild to moderated pain intensity was contributed due to no significant group difference. At the conclusion of treatment, both groups had improved function and decreased pain. After 3 months of treatment with GS/CS in combination with manual therapy have demonstrated significant improvement at baseline and at various intervals as compared to placebo [11]. In osteoarthritis management glucosamine and chondroitin sulfate show long lasting effects in pain reduction but they have slower onset of action [12, 13]. In one study it was observed that NSAID (Celecoxib) has superior effects in OA pain reduction as compared to glucosamine when used for 1-4 months but after 6 months results showed that both groups have similar effects (when evaluated on WOMAC scale & VAS of Huskisson) on intensity of pain and functional mobility of patients [14]. Several researched showed that supplements of GS/CS are more beneficial for OA patients. When administered for period of 3 years with dose of 1500mg per day revealed no further reduction in joint space of patient and improvement on WOMAC scale of OA [15]. Another study depicted that 2000mg per day of GS/CS use for 12 weeks has improved patient's quality of life and self-reported reduction in routine pain perception as well [16]. It was reported by some authors that 1500mg/d of

glucosamine Chondroitin or MSM use for 12-weeks intervals has analgesic and anti-inflammatory effects and showed reduction in patient's pain and enhanced QoL along with functional independence in mild to severe form of OA [17]. The results of our study are supported by above mentioned studies. Therapeutic exercise programs have also aided in symptom management of OA participants. ACSM (American college of sport medicine) has published some guideline for OA management e.g static stretching for enhancing patients muscle flexibility, aerobic exercises (around Vo<sub>2</sub> max of 40-60% for half an hour, for 3-5days per week, resistance exercises of low intensity (10-12 reps Or 40-60% or one repetition maximum for 2-3 times/day) involve major muscles [18]. In overweight and obese patient regular exercises have also showed improvement in patient balance, functional mobility & quality of life. Therefore, weight reduction are also thought to be beneficial for symptoms management of OA [19, 20].

## CONCLUSION

The GH/CS plus Physical therapy was found to be superior in the management of knee OA than just glucosamine chondroitin in reference to patient's function, pain, or mobility.

## Conflicts of Interest

The authors declare no conflict of interest

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