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Comparative study of oral native collagen type 2 versus oral glucosamine sulphate in patients with grade 2 and grade 3 primary osteoarthritis of the knee

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Abstract: Background: Osteoarthritis (OA) is a degenerative joint disease that affects the cartilage and surrounding tissues. This study aimed to compare the efficacy of oral native collagen type 2 and oral glucosamine sulphate in patients with grade 2 and grade 3 primary knee osteoarthritis.
Materials and Methods: This was a randomized observational prospective study conducted on patients aged 30 years or above, of any gender, diagnosed with primary knee osteoarthritis of grade 2 and 3. The patients were randomly assigned to two groups using computer randomization software. Group 1 received native type 2 collagen 40 mg (Tablet Dupact 40 mg, Wockhardt Limited), while Group 2 received oral glucosamine 1500 mg (Lubrijoint 750 mg twice daily).
Results: The majority of participants in the Glucosamine group were in the 51-60 years age group (32.5%), while the majority in the Collagen group were slightly younger, belonging to the 41-50 years age group (30%). The mean age of the Glucosamine group (57.2 $\pm$ 10.45 years) was similar to the Collagen group (57.2 $\pm$ 11.39 years), and the difference was not statistically significant. The pre-treatment and post-treatment (after 12 weeks) C-reactive protein (CRP) values did not show a statistically significant difference between the two groups. However, both the Glucosamine and Collagen treatments resulted in a significant reduction in WOMAC score and visual analog scale (VAS) score over the course of the 12-week treatment.
Conclusion: Both Glucosamine and Collagen treatments showed improvements in reducing painful and swollen joints, as well as significant improvements in VAS and WOMAC scores.

Keywords: Osteoarthritis; Native collagen type 2; WOMAC scores.

1. Introduction

Osteoarthritis (OA) is defined as a degenerative joint disease involving the cartilage and many of its surrounding tissues. In addition to damage and loss of articular cartilage, there is remodeling of sub articular bone, osteophyte formation, ligamentous laxity, weakening of periarticular muscles, and, in some cases, synovial inflammation [1,2].

The key to understanding OA is that the joint is a mechanical structure and OA is an abnormal mechanical stress. Joint failure is the pathophysiological response of a synovial joint to mechanical insult, and the attempt of the joint to repair the damage caused by local abnormalities in force/ unit area. The abnormalities in cytokines, degradative enzymes and toxic radicals which are being studied as the cause of OA, are rather the result of this attempted repair [3,4].

Though the disease progression is usually slow it can ultimately lead to joint failure and hence there is a dire need to find new approaches to control the disease progression and the symptoms associated with it but these advances will only come if we use the biological approaches along with biomechanics. Proof of concept studies are available which show that improvements that can occur in both symptoms and joint pathology

following osteotomy or joint distraction to unload damaged areas of the joint [5]. Present study was aimed to compare oral native collagen type 2 versus oral glucosamine sulphate in patients with grade 2 and grade 3 primary osteoarthritis of the knee.

2. Material and methods

Present study was Randomized observational prospective study, conducted in department of Orthopaedics, at Christian Medical College and Hospital, Ludhiana, India. Study duration was of 18 months (January 2021 to June 2022). Study approval was obtained from institutional ethical committee.

2.1. Inclusion criteria

Patients of age = 30 years, either gender, diagnosed as Primary Knee Osteoarthritis of Grade 2 and 3, willing to participate in present study

2.2. Exclusion criteria

- Patients with other Rheumatologic disorders causing inflammatory arthritis of the knee.
- Patients with Secondary OA
- Patients on supplements like Chondroitin Sulphate or other natural health products.
- Patients who had received intra articular hyaluronate, or systemic or intra-articular glucocorticoids .
- Patients who have severe cardiac, renal, hepatic or hematologic disease and pregnant women.

Study was explained to patients in local language & written consent was taken for participation & study. Demographic details, medical / past/ personal / family history, clinical details (complaints, examination findings), laboratory/radiological findings were noted in proforma. Blood CRP levels were sent at the start of the study and repeated at the end of the study. Patients were randomised into either of the two groups using a computer randomization software.

Group 1 was treated with Native type 2 collagen 40 mg [Tablet Dupact 40 mg, Wockhardt Limited], one tablet daily dose, and Tablet Paracetamol 650 mg for initial 7 days with physiotherapy and life style modification. After 7 days, only Native Type 2 collagen was continued along with physiotherapy and life style modification for 3 months.

Group 2 was treated with oral Glucosamine 1500 mg [Lubrijoint 750 mg twice daily +Tablet Paracetamol 650 mg for the initial 7 days with physiotherapy and life style modification. No other treatment for OA knee were allowed during the course. After 7 days, only Glucosamine was continued along with physiotherapy and life style modification for 3 months

Both the groups were followed up until completion of 3 month treatment course. Physiotherapy exercises and life style modification were advised to both the groups. Knee pain status of the patients were assessed at the beginning of the study, after 2 weeks, 4 weeks, 8 weeks and 12 weeks with VAS (Visual Analogue Scale) Score.OA associated symptoms were assessed by the Western Ontarion and McMaster Universities (WOMAC) osteoarthritis index. WOMAC scores were assessed at the beginning of the study, after 2 weeks, 4 weeks, 8 weeks and 12 weeks. WOMAC score of joint pain was the primary outcome measure. WOMAC scores of stiffness, limitation of physical function and patients' global assessment of disease severity and occurrence of adverse events were secondary outcome measures.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.05 was considered as statistically significant.

3. Results

In present study, majority of the study participants in the Glucosamine group belonged to 51-60 years (32.5 %), while majority of the study participants in the Collagen group were slightly younger than the Glucosamine group, belonging to 41-50 years age group (30 %). Mean age of the glucosamine group (57.2 $\pm$ 10.45 years) was similar to the collagen group (57.2 $\pm$ 11.39 years), difference was not statistically significant. There were more

females in the collagen group, and this difference was not statistically significant. We found that between the two groups, the distribution of co-morbidities didn't show any statistical difference.

The most common complaint in both the groups was found to be pain in the affected knee followed by swelling. The duration of complaints between the two groups was comparable, difference was not statistically significant. Right side was more involved in the collagen group, the difference was not statistically significant.

Table 1. General characteristics

	Glucosamine	Collagen	p value
Age groups (in years)			
31-40	2 (5 %)	4 (10 %)	
41-50	11 (27.5 %)	13 (32.5 %)	
51-60	12 (30 %)	8 (20 %)	
61-70	8 (20 %)	6 (15 %)	
71-80	6 (15 %)	7 (17.5 %)	
>80	1 (2.5 %)	2 (5 %)	
Mean age (mean ± SD)	57.2 ± 10.45	57.2 ± 11.39	0.094
Gender			0.165
Male	18 (45 %)	12 (30 %)	
Female	22 (55 %)	28 (70 %)	
COMORBIDITIES			0.464
Type 2 diabetes mellites	6 (15 %)	8 (20 %)	
Hypertension	9 (22.5 %)	7 (17.5 %)	
Complaints			
Pain	35 (87.5 %)	32 (80 %)	
Swelling	25 (62.5 %)	26 (65 %)	
Reduced range of movements	20 (50 %)	18 (45 %)	
Duration of complaints	44.68 ± 38.86	44.25 ± 38.8	0.955
Laterality			
Left	20 (50 %)	16 (40 %)	
Right	20 (50 %)	24 (60 %)	

We compared the pre-treatment and post-treatment (after 12 weeks) CRP values between the two groups, the difference was not statistically significant.

Table 2. Comparison between pre & post-treatment CRP levels

CRP	Glucosamine	Collagen	p value
Pre-treatment	3.818 ± 1.546	3.835 ± 1.724	0.9620
Post-treatment	3.214 ± 1.332	3.347 ± 1.543	

We found a significant reduction in the WOMAC score with Glucosamine treatment. We found a significant reduction in the WOMAC score with Collagen treatment over the course of the 12 week treatment. When we compared the WOMAC scores at week 12 between the two treatment groups, we found that there was no statistically significant difference.

Table 3. Comparison of WOMAC scores over the course of the treatment

	Glucosamine	Collagen
Pre-treatment	79.925 ± 9.4906	80.925 ± 7.4949
Week 2	66.65 ± 11.0745	72.45 ± 11.1377
Week 4	39.85 ± 8.8508	48.925 ± 15.5965
Week 8	26.3 ± 3.9626	25.875 ± 3.8041
Week 12	20.2 ± 3.7703	20.2 ± 3.7703
p value	<0.0001	<0.0001

When we compared the VAS scores within the two groups to analyze the best improvement in the pain, we found a significant reduction in the VAS score with Glucosamine treatment. We found a significant reduction in the VAS score with Collagen treatment. When we compared the VAS scores at week 12 between the two treatment groups, we found that there was no statistically significant difference.

Table 4. Comparison of VAS scores over the course of the treatment

	Glucosamine	Collagen
Pre-treatment	8.075 ± 0.7642	7.275 ± 0.5986
Week 2	7.3 ± 0.6076	6.075 ± 0.7299
Week 4	6.075 ± 0.6938	4.875 ± 0.5633
Week 8	4.925 ± 0.6155	3.525 ± 0.64
Week 12	2.78 ± 0.62	2.925 ± 0.6558
p value	<0.0001	<0.0001

When we correlated the requirement of rescue analgesia between the two group, we observed that it was lesser in the collagen group, this difference was not statistically significant. (The chi-square statistic is 1.1712. The p-value is .759926. The result is not significant at $p < .05$.)

Table 5. Requirement of rescue analgesia

Rescue analgesia	Glucosamine	Collagen	p value
Week 2	21 (52.5 %)	19 (47.5 %)	0.759
Week 4	19 (47.5 %)	13 (32.5 %)	
Week 8	14 (35 %)	7 (17.5 %)	
Week 12	4 (10 %)	3 (7.5 %)	

At end of week 2, mean joints with pain was higher in Glucosamine group, but the mean joints with swelling were found to be higher in Collagen group. However, this difference was not statistically significant. The mean VAS score was found to be lower in the Collagen group then the Glucosamine group, which was statistically significant. The mean WOMAC score was found to be lower in the Glucosamine group then the Collagen group, which was statistically significant.

Table 6. Comparison of joints (painful and swollen), VAS & WOMAC at week 2

	Glucosamine	Collagen	p value
Total joints with pain	1.53 ± 0.82	1.44 ± 0.89	0.912
Total joints with swelling	1.42 ± 0.77	1.67 ± 0.92	0.834
VAS	7.3 ± 0.61	6.07 ± 0.73	<0.0001
WOMAC	66.65 ± 11.07	72.25 ± 11.13	<0.0001

Mean joints with pain and swelling was higher in Glucosamine group than collagen groups at week 4 of follow-up, difference was not statistically significant. The mean VAS score was found to be lower in the Collagen group then the Glucosamine group, which was statistically significant. The WOMAC score was found to be lower in the Glucosamine group than Collagen, and this difference was also found to be statistically significant.

Table 7. Comparison of joints (painful and swollen), VAS & WOMAC at week 4

	Glucosamine	Collagen	p value
Total joints with pain	1.23 ± 0.68	1.12 ± 0.67	0.821
Total joints with swelling	1.35 ± 0.72	1.24 ± 0.75	0.845
VAS	6.01 ± 0.69	4.87 ± 0.56	<0.0001
WOMAC	39.85 ± 8.85	48.92 ± 15.59	<0.0001

4. Discussion

The osteoarthritic population is the most neglected patient population worldwide. According to the World Health Organization, OA is among the top ten conditions in the global burden of disease [6]. The knee is one of the joints most frequently affected by OA [7]. It is the most common form of arthritis, and has enormous implications in terms of personal suffering and costs to society [7]. The most important change in OA over the past 60 years has been in attitudes rather than knowledge [6]. Though there are a few health care professionals and patients who have accepted this change it is not fully accepted by people associated with OA worldwide.

The radiological definition of OA has been used in various studies using the Kellgren and Lawrence score [8]. The overall grades of severity are determined from 0 to 4 and are related to the presumed sequential appearance of osteophytes, joint space loss, sclerosis and cysts [9]. Clinical OA is defined by features in the history and on examination. It invariably requires the presence of joint pain in addition to other features. Though there is a correlation between the severity of radiographic disease and symptoms, the association is not strong [10].

In our study, we found that the patients in the glucosamine group was 51-60 years, while they were slightly younger in the collagen group. In a study by T Trc *et al*., [11] we found the similar findings to our study. In a study by Jordi Puigdellivol *et al*., [12] we observed that the study participants were also predominantly above 40 years age. In a study by D C Crowley *et al*., [13] the mean age of the study participants was similar to our study.

In our study, we found that majority of the study participants were females. In the study by T Trc *et al*., [11] Jordi *et al*., [12] and D C Crowley *et al*., [13] there were similar findings, however, in a study by Deal CL *et al*., [14] the M:F ratio was nearly 1:1.

In the present study, we find that there is a statistically significant difference in the WOMAC scores over the course of 8 weeks within the Glucosamine and Collagen group independently. We also observed a statistically significant difference between the two groups on follow up at week 2 and 4, but not at week 12.

In research by D C Crowley *et al*., [13] the interaction between visit and therapy was significant for "pain walking on flat surface" (p=0.034), "difficulty walking on flat surface" (0.038), and "doing heavy household activities" (0.031). UC-II therapy was much better than G+C for "ascending stairs" (p=0.013). When groups were evaluated at each visit, UC-II was significantly superior than G+C for "ascending stairs at 30 days and 60 days" (p=0.019 & 0.040 respectively), "at night while in bed" (p=0.015) at 60 days, and difficulty walking on level surface at 90 days (p=0.035). No other WOMAC components or summary scores differed statistically. UC-II reduced WOMAC scores by 33% compared to 14% in (G+C)-treated groups after 90 days. Within-group analysis showed that 90-day UC-II treatment improved WOMAC scores at all time points ($p<0.05$). G+C treatment did not significantly affect WOMAC scores at Day 90.

In the present study, we find that there is a statistically significant difference in the VAS scores over the course of 12 weeks within the Glucosamine and Collagen group independently. We also observed a statistically significant difference between the two groups on follow up at week 2 and 4, but not at week 12.

D C Crowley *et al*., [13] found no interaction between visit and treatment for VAS components or summary scores. UC-II treatment significantly reduced "pain during climbing up and down stairs," "night pain," and "resting pain" (p=0.035, 0.030, and 0.024). In 60 days and 90 days, UC-II was considerably superior than G+C for "night pain" (p=0.040) and "resting pain" (p=0.020). No VAS component or summary score differed between groups. UC-II lowered the VAS score by 40% after 90 days, compared to 15% for G+C.

According to the results of our research, the analgesic potential of collagen was non-inferior to Glucosamine. It was also shown to be non-inferior to glucosamine in terms of alleviating pain and increasing WOMAC score. Because of this, increasing the quantity of food does not result in an increase in the number or severity of adverse effects, and in reality, there was no significant statistical difference between the adverse effects caused by Glucosamine and Collagen after 2, 4, 8 or 12 weeks of sequential administration. In addition, there was no statistically significant variations between the amounts of rescue analgesia that were administered when comparing Glucosamine and Collage.

We observed that initially, collagen out-performed Glucosamine with respect to reduction in pain and WOMAC scores. However, a slight difference was seen in week 4. However, at the conclusion of 12 weeks

treatment with both the groups, we find that Collagen brings about the similar reduction in pain and WOMAC as Glucosamine.

Both native collagen type 2 and glucosamine are effective in treatment of osteoarthritis of knees, but collagen can be used in patients who are not compliant to glucosamine due to side effects, especially in diabetic patients. Oral native collagen type 2 is a newer nutraceutical for the treatment of Osteoarthritis of the knees and there are only few studies from India which evaluated its efficacy in comparison to glucosamine sulphate. This study can add to evidence on the effectiveness of both oral native collagen type 2 and glucosamine sulphate in improving the pain and joint function in OA knees.

Limitations of present study were small sample size, limited duration of the study & this study only highlights the results based on VAS score and WOMAC score.

5. Conclusion

Glucosamine and Collagen can reduce the number of painful and swollen joints, as well as have a significant improvement in VAS and WOMAC scores. Native collagen type 2 and Glucosamine are equally efficient and have similar beneficial effect in patients with grade 3 OA knees. Both collagen type 2 and glucosamine sulphate improve the pain and joint function in patients with knee OA, beneficial in patients unfit for surgery to improve symptoms such as pain and swelling and can decrease requirement of paracetamol consumption.

6. Conflict of Interest

None to declare

7. Source of funding

Nil

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