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A Clinical Study on Glucosamine Sulfate Versus a Combination of Glucosamine Sulfate and NSAID Drug in Knee Osteoarthritis

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Sathishkumar R*, Charumathi A, Babisha J, Suganthi S, Sankar C

Department of Pharmacy Practice, KMCH college of Pharmacy, Kovai Estate, Kalapatti Road, Coimbatore-641048, Tamil Nadu, India (Affiliated to The Tamil Nadu Dr. M.G.R. Medical University).

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ABSTRACT

Background: This study was aimed to assess and ensure the safety and efficacy of glucosamine sulfate compared with a combination of glucosamine sulfate and Non-Steroidal Anti-Inflammatory Drug (NSAID) in mild to moderate knee osteoarthritis (OA). **Objectives**: The basic objective of the study is determining the effectiveness of glucosamine sulfate in reducing joint pain in mild to moderate knee OA and assessing the effectiveness of glucosamine sulfate in improving the joint physical function from mild to moderate knee OA. **Materials and methods**: The patient data were obtained through Patient case sheet, WOMAC (Western Ontario McMaster Universities) index of osteoarthritis questionnaires,Visual analog scale (VAS). The WOMAC scale is a disease-specific self-administered health status measures that are widely accepted as a reflective of osteoarthritis disease activity. Patients marked on the linear scale the relevant amount of pain they were experiencing and the value was noted.**Results**: In total 143 patients were interviewed.100 subjects with OA of the knee were randomized and divided into two groups. 18 subjects were dropped out from the study because they were lost to follow up and refused further therapy.8 subjects due to poor compliance (3 GS, 5GS+NASID), 6 due to gestational upset (GS+NSAID) And 4 due to inadequate pain control (GS)]. Finally, 82 subjects have completed in the study.**Conclusion**: This study results may suggest that the glucosamine sulfate has a carry-over effect like a disease-modifying agent. Long term treatment of GA is preferred to improve the quality of life of patients.

1. INTRODUCTION

Osteoarthritis (OA) is one of the most common disabling joint disorders in adults. Approximately one in every seven adults suffers from this condition over their lifetime, with 9% of the USA population affected by the age of 60. Furthermore, by the year 2030, arthritis is predicted to affect up to 25% of the US adult population and limit activity at 9.3%. Osteoarthritis is also economically burdensome due to the high prevalence, growing treatment expenditures, and substantial indirect costs of the disease. National studies in industrialized countries have appraised the economic impact of arthritis as 1.5–2.5% of the irrespective gross national products (GNP) [1].The management of OA in the TMJs can include splint and physical therapy, corticosteroid injections, and orally administered medication, most often a nonsteroidal anti-inflammatory drug (NSAID). In addition to not being proven effective for TMJ pain, including OA, the use of repeated doses of NSAIDs has the potential to produce serious gastrointestinal and renal toxicity, which limits their use. Because concern has been raised about the safety of existing pharmacologic management, there is a need for new and effective oral treatment of OA. Glucosamine appears to be an attractive alternative because it is a naturally occurring compound in the auricular cartilage [2].Disease-modifying agents are not yet available in usual care, although there has recently been a lot of debate about some biological agents that are thought to have both symptoms – modifying and disease-modifying properties results from previous trials have not been convincing. Of these biological agents, glucosamine sulfate seems to be the most promising[3].Glucosamine, which occurs naturally in the body, plays a key role in the construction of cartilage (the tough connective tissue that cushions the joints). Glucosamine is the most fundamental building block required for the biosynthesis of the classes of compounds including glycolipids, glycoproteins, hyaluronate, and proteoglycans[4]. As the component of these macromolecules glucosamine has a role in the synthesis of the cell membrane, lining, collagen, and bone matrix. Glucosamine is also required for the formation of lubricants and protective agents such as mucin and mucous secretion[5].

2. METHODOLOGY

This study was carried out in Kovai Medical Center and Hospital, Coimbatore. It is a multi-specialty corporate hospital.This study was a prospective, open-label, pilot study.The study was conducted for 6 months.

The patients who were included in the study are

- Patients diagnosed with knee osteoarthritis.
- Male and female patients above 18 years of age.

The patients who were excluded from the study are

- Rheumatoid arthritis patients
- Joint replacement knees
- History of chronic infection such as hepatitis, COPD, etc

The study population of a total of 143 subjects was interviewed, 100 qualified, 82 completed the study. Out of which 43 subjects were Group A (only glucosamine sulfate) and 39 subjects were in group B (glucosamine sulfate + anyone NSAID). The data were collected from the following sources:

- Patient case sheet
- WOMAC (Western Ontario McMaster Universities) index of osteoarthritis questionnaires.
- Visual analog scale (VAS)

2.1. Outcome measures

2.1.1. Primary efficacy variables

The WOMAC scale is a disease-specific self- administered health status measures that are widely accepted as a reflective of osteoarthritis disease activity 46. The original index consists of 24 questions, there are three sections to the WOMAC score, section A consists amount of pain(5 questions), section B address the amount of joint stiffness (2 questions), section C consists of physical function (17 questions). Subjects were allowed to answer these questions and the responses were noted[6].

2.1.2. Secondary efficacy variable

VAS- visual analog scale score uses a 100 mm (10 cm) linear measure of pain status with 0 representing no pain and 100 being unbearable pain47. Patients marked on the linear scale the relevant amount of pain they were experiencing and the value was noted[7].

2.2. Statistical analysis

Documented data were entered in SPSS VERSION 10. Within the group, the variables were compared with a paired t-test. Between groups were compared with independent t-test. Statistical significance was taken at the 95% confidence interval .results were expressed as Mean ± Standard deviation (SD).

3. RESULTS AND DISCUSSION

In total 143 patients were interviewed.100 subjects with OA of the knee were randomized and divided into two groups. All the subjects were received trail medication immediately after randomization. 18 subjects were dropped out of the study because they were lost to follow up and refused further therapy.[8] subjects due to poor compliance (3 GS, 5GS+NASID), 6 due to gestational upset (GS+NSAID) And 4 due to inadequate pain control (GS)]. Finally, 82 subjects have completed in the study. Among the study subjects the mean age of the female subject (47.96± 5.09 and 48.95 ± 8.94) was lower than the male subjects in group A and group B. out of 82 subjects studied, the percentages of female subjects were greater than the percentage of male subjects i.e.., 60.49% and 53.84% respectively in group A and group B.The subjects with the age groups of 41-50 years and 51-60 years were the highest in number by 21 (48.83%) and 19 (44.18%)in group A. 14 (35.89%) in group B. among the patients 10 (23.25%), 5(12.82%) were affected by left knee OA, 11(25.58%), 12(30.76%) were affected by right knee OA and 22(51.62%), 22(56.41%) were affected by bilateral knee OA in group A and group B.

The mean BMI ratio of subjects was noted under the overweight category. In group A, 25.6 were noted both in male and female. In group B 25.83and 26.48 were noted in the male and female category. The mean WOMAC pain score difference between group A and group B shows that the mean difference was 4.20 (95% confidence interval) on the first review. The mean difference was 5.37 (95 % confidence interval) on the last review. The results revealed that the significant mean difference between group A and group B ($p<0.01$).Between the

group analysis, the results show that the mean difference was 1.35 on the first review. The mean difference was 2.23 on last review **(table.1).**

Table No. 1: Comparison of WOMAC stiffness mean score between group A and group B

REVIEW	MEAN DIFFERENCE	95 % CI OF THE DIFFERENCE		t- value
		Lower	Upper	
o week	0.2689	0.6406	0.0960	1.444
4 weeks	1.3584	1.1049	1.1611	10.686
8 weeks	1.6971	1.1414	1.9792	12.015
12 weeks	2.2308	2.2130	2.4402	21.333

The results revealed that the significant mean difference between groups A and B ($p<0.01$). Between the groups, analysis results show that the mean difference was 7.56 on the first review. The mean difference was 8.20 on the second review after 12 weeks (**table.2**).

Table No. 2: Comparison of WOMAC function mean score between group A and group B

REVIEW	MEAN DIFFERENCE	95 % CI OF THE DIFFERENCE		t- value
		Lower	Upper	
o week	1.0781	2.0817	0.00745	2.139
4 weeks	7.5635	1.8305	16.9575	1.624
8 weeks	5.8968	5.0456	6.7481	13.797
12 weeks	8.2027	7.5122	8.8933	23.745

These results revealed that the significant mean difference between group A and B ($p<0.01$). Between the group analysis results shows that the mean difference was 8.45 on the first review. The mean difference was 15.78 after 12 weeks (**table 3**).

Table No. 3: Comparisons of WOMAC total mean score between group A and group B

REVIEW	MEAN DIFFERENCE	95 % CI OF THE DIFFERENCE		t- value
		Lower	Upper	
o week	3.1181	4.7903	1.4458	3.712
4 weeks	8.452	6.9091	9.9949	10.975
8 weeks	11.7847	10.4513	13.1181	17.603
12 weeks	15.7865	14.681	16.8921	18.659

Thus the results revealed that the significant difference between groups A and B ($p<0.01$).Between the groups, analysis results showed that the mean difference was 0.79 on the first review. The mean difference was 1.12 on last review (**table.4**).

Table No. 4: Comparison of pain mean score between Group A and Group B

REVIEW	MEAN DIFFERENCE	95 % CI OF THE DIFFERENCE		t- value
		Lower	Upper	
o week	-0.5668	0.8652	0.2654	3.743
4 weeks	0.7897	0.5625	1.017	6.936
8 weeks	0.8927	0.5841	1.02013	5.764
12 weeks	1.1261	0.8369	1.4127	7.824

These results revealed that the significant means difference between group A and B ($p<0.01$).In this study period 7 (14%) subjects were reported side effects in group A and 12 (24%) were reported side effects in group B (**table.5**). from that 9 (18%) subjects GI upset as side effect in group B in that 6 (12%) subjects were discontinued from the study.

Table No. 5: SIDE EFFECTS

SIDE EFFECTS	GROUP A (n=43)	GROUP B (n=39)
Nausea /vomiting	2	3
GI upset	1	9
Tenderness in knee	2	0
Bloating	2	1

4. CONCLUSION

The results from the first review revealed that the combination of GS with NSAID showed better improvement in pain, stiffness and physical function compared with the glucosamine alone group. This study results may suggest that the glucosamine sulfate has a carryover effect like a disease-modifying agent. Long term treatment of GA is preferred to improve the quality of life of patients.

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