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Original Research Article

Prospective observational study on effectiveness of glucosamine, diacerein, and methyl sulfonyl methane on osteoarthritis

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ABSTRACT

Background: Some research studies showed that nutraceuticals like glucosamine, chondroitin, methyl-sulfonyl-methane etc, are showing effectiveness in treating osteoarthritis (OA). But there is no proper evidence that these drugs can treat OA because some research studies also showed, these nutraceuticals have little to no effect in OA. The main purpose of our study is to take a combination of nutraceuticals, which are glucosamine, diacerein and methyl-sulfonyl-methane and find the effectiveness of these nutraceuticals in treating OA.
Methods: In this prospective study, 194 subjects were taken and conducted an observational study. Numerical pain rating scale (NPRS) was used to assess pain severity and X-ray is used to assess the joint space narrowing. Based on pain severity, subjects are divided into three groups i.e., mild, moderate and severe and given the treatment of glucosamine, diacerein, and methyl-sulfonyl-methane and reviewed.
Results: From the analysis of NPRS score, on admission, patient severity was severe 97%, moderate 3% and mild pain was 0%, and after three reviews over a period of 6 months, the pain severity of patients was severe 8.76%, moderate 87.1% and mild pain was 4.12%.
Conclusions: Based on our study we concluded that glucosamine, diacerein, and methyl-sulfonyl-methane can effectively treat OA by repairing the damaged articular cartilage. But these medications cannot produce new articular cartilage, they only repair the damaged articular cartilage.

Keywords: Glucosamine, Diacerein, Methyl-sulfonyl-methane, OA, Articular cartilage, Nutraceuticals

INTRODUCTION

Osteoarthritis (OA) is a long-term chronic disease characterized by the deterioration of the cartilage in joints which results in bones rubbing together and creating stiffness, pain, and impaired movement. The disease most commonly affects the joints in the knees, hands, feet, and spine and is relatively common in the shoulder and hip joints. While OA is related to aging, it is also associated with a variety of both modifiable and non-modifiable risk factors, including obesity, lack of exercise, genetic predisposition, bone density, occupational injury, trauma, and gender.[1]

Treatment of OA

Pharmacological treatment

Drugs

Analgesics are used mainly to suppress pain. A trial of different drugs is carried out to find a suitable drug for a

particular patient. The long-acting formulations are preferred.

Chondroprotective agents

Agents such as glucosamine and chondroitin sulphate have been introduced, claiming to be the agents that result in repair of the damaged cartilage. Their role as disease-modifying agents has yet not been established, but these could be tried in some early cases.

Visco-supplementation

Sodium hyaluronate has been introduced. It is injected in the joint 3-5 times at a weekly interval. It is supposed to improve cartilage functions and is claimed to be chondroprotective.

Supportive therapy

This is a useful and harmless method of treatment and often gives gratifying results. It consists of the following: Weight reduction, in obese patients, avoidance of stress and strain to the affected joint in day-to-day activities. For example, a patient with OA of the knee is advised to avoid standing or running whenever possible. Sitting cross-legged and squatting is harmful to OA of the knee, local heat provides relief of pain and stiffness, exercises for building up the muscles controlling the joint help in providing stability to the joint. The local application of counter-irritants and liniments sometimes provide dramatic relief.

Now a days, the following three drugs are frequently used by clinicians to treat OA. They are: Diacerein, glucosamine, methyl-sulfonyl-methane

Diacerein

The principal mechanism of action of diacerein is to inhibit the interleukin-1b (IL-1b) system and related downstream signalling.[10] Diacerein has been shown to impact the activation of IL-1b via reduced production of IL-1 converting enzyme, as well as to affect the sensitivity to IL-1 by decreasing IL-1 receptor levels on the cell surface of chondrocytes and by indirectly increasing IL-1 receptor antagonist production.[11-13]

Production of IL-1b may also be affected, as diacerein has been shown to inhibit the IL-1b-induced activation of transcription factor NF-jB, which stimulates pro-inflammatory cytokine expression. Down-regulation of IL-1 levels has been confirmed in the synovial fluid of patients with knee OA. Besides its anti-inflammatory properties, diacerein has been shown to have anti-catabolic and pro-anabolic effects on cartilage and synovial membrane, as well as protective effects against subchondral bone remodelling.[2-9]

Glucosamine

Glucosamine is an amino sugar synthesized from glucose and glutamine. It is a source of glucosamine-6-phosphate and N-acetylglucosamine. It is an intermediate compound, converted to an ester that is incorporated into articular cartilage. Therefore, it is a direct precursor in the formation of glycosaminoglycans in cartilage. Glucosamine is usually administered as a combination of glucosamine HCL and chondroitin sulfate. Other forms include glucosamine sodium sulfate and glucosamine potassium sulfate. Glucosamine has been promoted to stimulate the synthesis of synovial fluid, inhibit degradation, and improve the healing of articular cartilage.

Oral absorption may be affected by the form administered because glucosamine sulfate may be better absorbed than glucosamine hydrochloride.[14]

Methyl-sulfonyl-methane

Mechanism of action MSM has been proven to have anti-inflammatory and antioxidant mechanisms in an in vitro study in which human neutrophils were artificially stimulated to produce oxidative compounds, including hydrogen peroxide, superoxide, and hypochlorous acid. After cell lines were treated with either DMSO or $DMSO_2$, these free radical by-products were decreased.

Dosage oral dosage of MSM is often in the range of 1-3 grams daily; however, up to 18 grams per day have been used under medical supervision.[15]

MSM might cause nausea, diarrhoea, bloating, fatigue, headache, insomnia, itching, or worsening of allergy symptoms.[16]

Numeric pain rating scale

Purpose

The numeric pain rating scale (NPRS) is a unidimensional measure of pain intensity in adults, including those with chronic pain due to rheumatic diseases.[17-20]

Content

The NPRS is a segmented numeric version of the visual analogue scale (VAS) in which a respondent selects a whole number (0-10 integers) that best reflects the intensity of his/her pain.[19] The common format is a horizontal bar or line. Similar to the VAS, the NPRS is anchored by terms describing pain severity extremes.[21]

Number of items

Although various iterations exist, the most commonly used is the 11-item NPRS.[22]

Response options/scale

The 11-point numeric scale ranges from '0' representing one pain extreme (e.g., "no pain") to '10' representing the other pain extreme (e.g., "pain as bad as you can imagine" or "worst pain imaginable").[18-19]

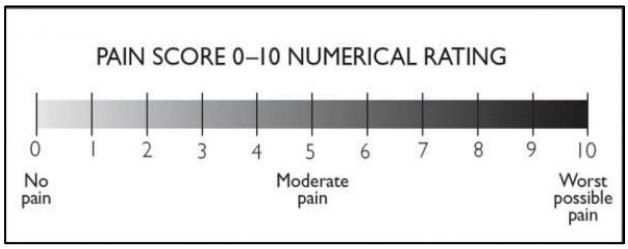

Figure 1: NPRS.

Recall period for items

Recall varies, but respondents are most commonly asked to report pain intensity "in the last 24 hours" or average pain intensity.[23]

Administration

The NPRS can be administered verbally (therefore also by telephone) or graphically for self-completion. As mentioned above, the respondent is asked to indicate the numeric value on the segmented scale that best describes their pain intensity.[20-21]

Scoring and interpretation

Scores range from 0-10 points, with higher scores indicating greater pain intensity.[21]

Acceptability

Chronic pain patients prefer the NPRS over other measures of pain intensity, including the VAS, due to comprehensibility and ease of completion. However, focus groups of patients with chronic back pain and symptomatic hip and knee OA have found that the NPRS is inadequate in capturing the complexity and idiosyncratic nature of the pain experience or improvements due to symptom fluctuations.[24-26]

Validity

For construct validity, the NPRS was shown to be highly correlated with the VAS in patients with rheumatic and other chronic pain conditions (pain>6 months): correlations range from 0.86 to 0.95.[20]

Aim and objective

The study aim to evaluate the effectiveness of glucosamine, diacerein and methyl-sulfonyl-methane in OA patients and objectives were to assess the effectiveness of glucosamine, diacerein, methyl-sulfonyl-methane in treating OA patients, to study the descriptive epidemiology of OA, to assess glucosamine, diacerein, MSM in providing symptomatic relief and slow down the progression of cartilage damage, to find/identify the cartilage regeneration in OA patients and to improve patients quality of life.

Need of the study

OA is a common orthopedic disease that is mainly caused by aging, in both men and women. The most commonly used nutraceuticals to treat OA are glucosamine and methyl-sulfonyl-methane. Some of the studies shown that both glucosamine and methyl-sulfonyl-methane are ineffective.

But some other studies have shown that glucosamine and methyl-sulfonyl-methane was ineffective in treating minor pains associated with OA but they are only effective when the pain is moderate to severe. Since cartilage damage is seen in OA, Diacerein, an anthraquinone, has anti-OA and cartilage stimulating property. So, the need of the study is to evaluate the effectiveness of combined use of drugs like glucosamine, diacerein and methyl-sulfonyl-methane in OA.

METHODS

Study site

This study was conducted at ortho and trauma care hospital, Narasaraopeta. The patients who visit this hospital are usually from in and around the districts of Guntur and Prakasam.

Study design

A hospital-based prospective observational study.

Sample size

A total of 194 patients from the out-patient of the department of orthopaedics. Those who fulfilled the exclusion and inclusion criteria were selected for the study.

Study period

The study was conducted over 6 months.

Study criteria

The study will be carried out by considering the following criteria:

Inclusion criteria

The patients who are having OA, patients of both males and females above the age of 50 years and patients with other comorbid conditions are also included.

Exclusion criteria

Patients who had a history of asthma, patients who have shellfish allergy are excluded from the study, people undergoing total knee replacement surgery were excluded from the study.

Ethical approval

This study was approved by the institutional human ethical committee of Narasaraopeta institute of pharmaceutical sciences, Narasaraopeta.

Source of data

The patient's demographical data, clinical data, therapeutics data and various other relevant and necessary data were obtained every day from the medical records as well as the other relevant information sources are documented.

Data handling and management

The data collection form is enclosed. MS excel format will be used for collecting data. Strict privacy and confidentiality are maintained during data collection.

Study procedure

All the patients consulted to the department of orthopedics were reviewed daily to identify the pain severity and it is assessed by the NPRS. Those patients who met the study criteria were enrolled in the study. A suitable data collection form was designed to collect all the necessary and relevant information.

The demographic details of the patient such as name, age, sex; clinical data such as chief complaints, diagnosis, and clinical condition; therapeutic data such as name of the drugs, dose, route, frequency, duration of therapy and other relevant details were collected by reviewing the case sheets, treatment charts and by interviewing the patients. A note of other concomitant medications consumed was also made. A personal visit was made to all the patients who were included in the study to collect any further information. Their medications were cross-checked with the treatment chart. All the patients were monitored from the day of admission.

RESULTS

Figure 1 shows the age-based distribution of patients admitted in the orthopedic hospital. The 142 out of 194 patients were between 51-60 years of age "With 95% confidence the population means is between 40.7 and 56.3, based on 194 samples".

Figure 2 shows the Gender-based distribution of patients. Among them male were 42.27% (n=82) and female were 57.73% (n=112). OA is more common among females.

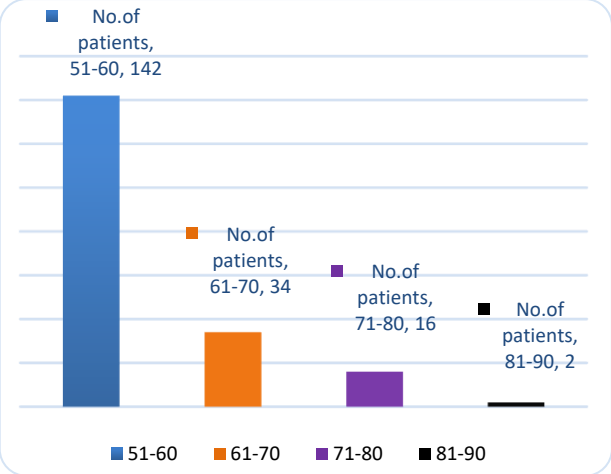

Figure 1: Age wise distribution.

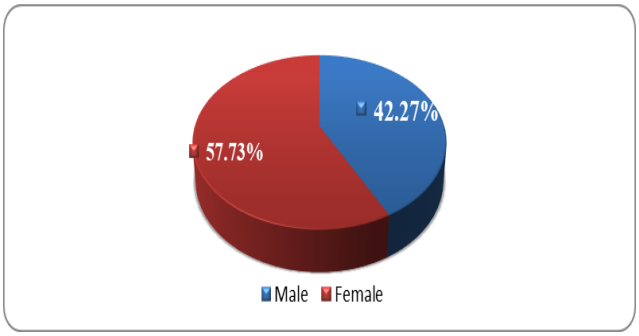

Figure 2: Gender-based distribution of patients.

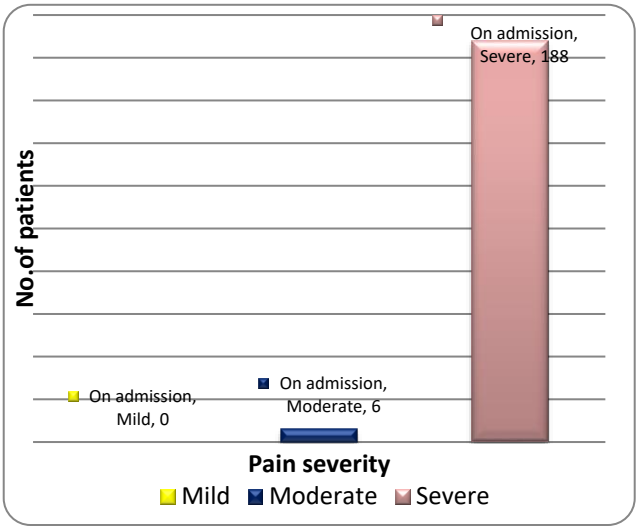

Figure 3: Severity based distribution on the admission of patients studied.

Figure 3 shows the severity-based distribution on admission of patients among them mild were 0% (n=0), moderate were3% (n=6) and severe were 97% (n=188).

Figure 4 shows severity-based distribution on pain severity of patients on admission and followup-1 of patients. Among them mild were 0% (n=0) patients on admission

and 1% (n=2) patients on followup-1, moderate were 3% (n=6) patients on admission and 38% (n= 73) patients on followup-1, severe were 97 % (n=188) patients on admission and 61% (n=119) on followup-1

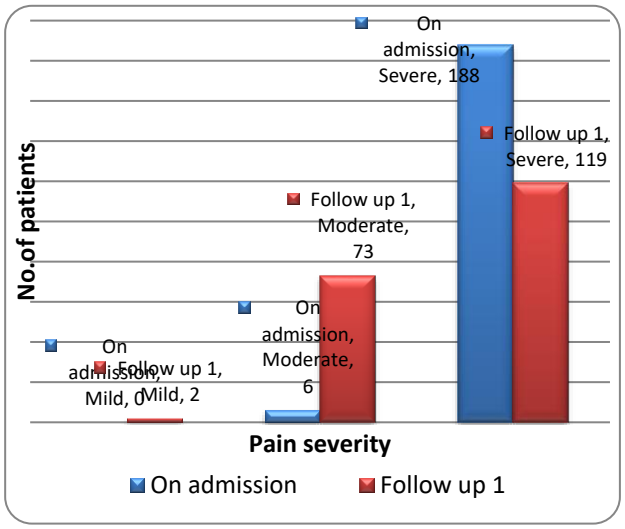

Figure 4: Distribution based on pain severity of patients on admission and followup-1.

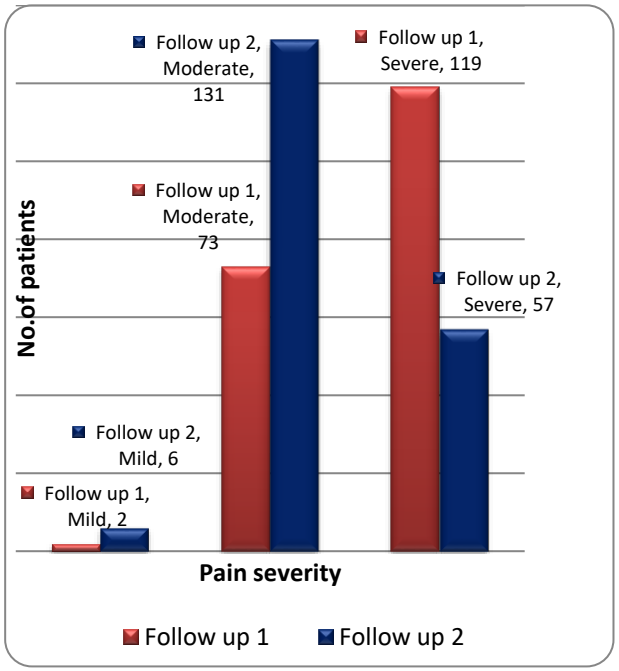

Figure 5: Distribution based on pain severity of patients in followup-1 and followup-2.

Figure 5 shows severity distribution based on the pain severity of patients in the followup-1 and followup-2. Among them mild were 1% (n=2) patients on followup-1and 3% (n=6) patients on followup-2, moderate were 38% (n=73) patients on followup-1 and 68% (n=131) patients on followup-2, severe were 61% (n=119) patients on followup-1 and 29% (n=57) on followup-2.

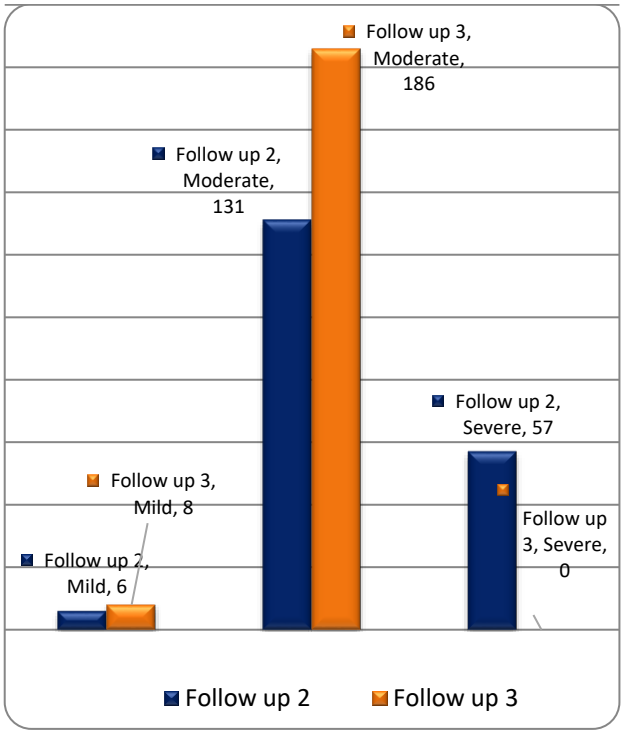

Figure 6: Distribution based on pain severity of patients in followup-2 and followup-3.

Figure 6 shows severity distribution based on the pain severity of patients in the followup-2 and followup-3. Among them mild were 3% (n=6) patients on followup-2and 4.12% (n=8) patients on followup-3, moderate were 68% (n=131) patients on followup-2 and 95.88% (n= 186) patients on followup-3, severe were 29% (n=57) patients on followup2 and 0% (n=0) on followup-3.

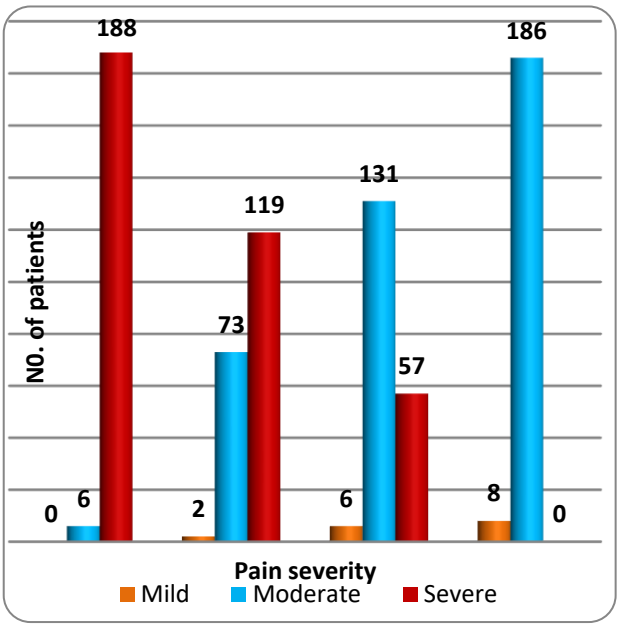

Figure 7: Distribution based on pain severity of patients in all followups.

Figure 7 shows distribution based on pain severity of patients in all follow-ups. Among them mild were 0 patients on admission, 2 patients on followup-1,6 patients on followup-2 and 8 patients on followup-3, moderate were 6 patients on admission,73 patients on followup-1, 131 patients on followup-2 and 186 patients on followup-3, severe were 188 patients on admission, 119 patients on followup-1, 57 patients on followup-2 and 0 on followup-3.

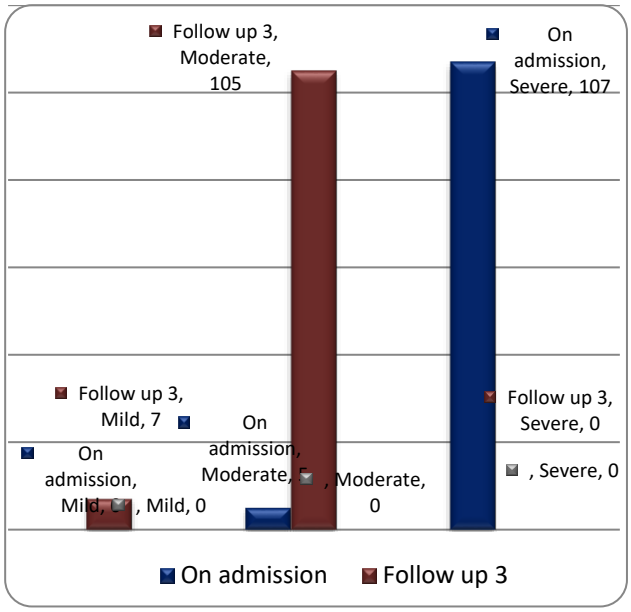

Figure 8: Distribution based on pain severity in females on admission and followup-3.

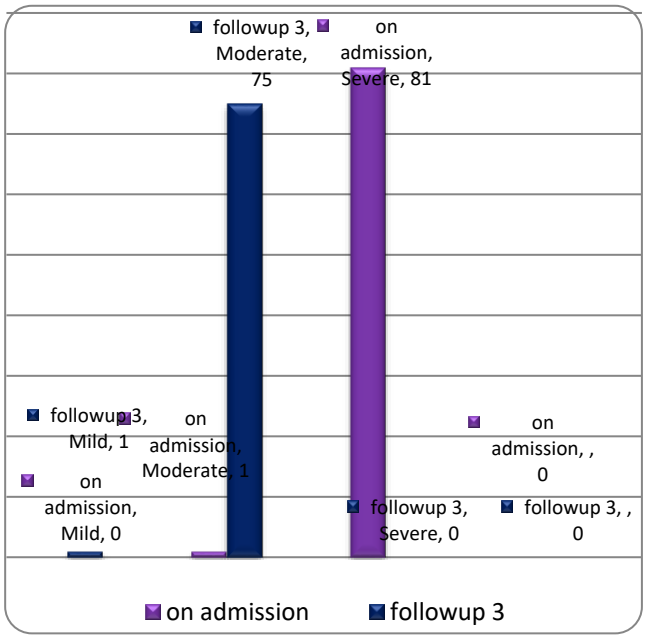

Figure 9: Distribution based on pain severity in males on admission and followup-3.

Figure 8 shows severity distribution based on the pain severity of female patients from admission to followup-3. Among them mild were 0% (n=0) patients on admission and 6.25% (n=7) patients on followup-3, moderate were 4.46% (n=5) patients on admission and 93.75% (n=105) patients on followup-3, severe were 95.53% (n=107) patients on admission and 0% (n=0) on followup-3.

Figure 9 shows severity distribution based on the pain severity of male patients from admission to followup-3. Among them mild were 0% (n=0) patients on admission and 1.21% (n=1) patients on followup-3, moderate were 1.21% (n=1) patients on admission and 98.78% (n= 81) patients on followup-3, severe were 98.78% (n=81) patients on admission and 0% (n=0) on followup-3

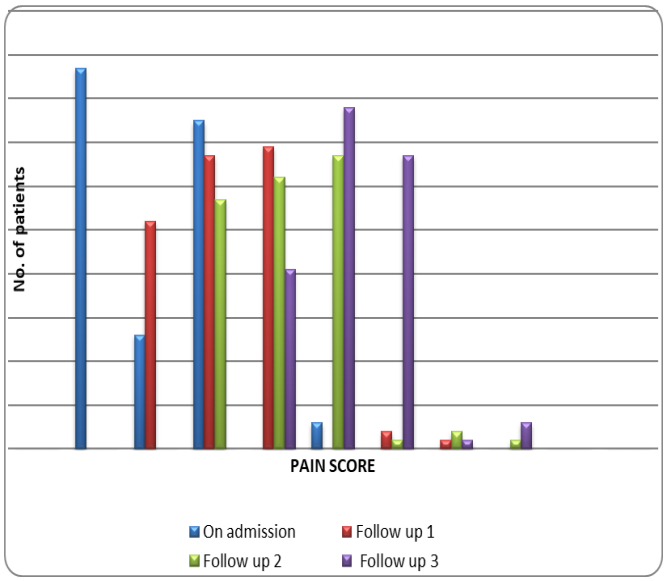

Figure 10: Distribution based on pain score of patients in all follow ups.

DISCUSSION

In this study, we performed a Prospective observational study on the Effectiveness of Glucosamine, Diacerein, and Methyl-sulfonyl-methane in OA. We recorded the pain severity of the subjects on admission by using the NPRS. We conducted three Follow-up to the subjects and recorded their pain severity. Based on the three follow-up's we concluded our study.

By using the N-master formula we calculated our sample size as 194. On admission out of 194 subjects, we got 194 cases as Knee OA. In India, as most of the epidemiological studies says that knee OA is more prevalent than any other OA. Because, in India, most of the people use Asian toilets, where people used to squat, which produces more pressure on knees and over time, upon years of doing may produce knee OA and in India, most of the people sit in a crossed-legged position, hence more amount of pressure experienced on their knees which may cause knee OA.

OA is a chronic degenerative disorder characterised by cartilage loss, it will develop over time, not immediately.[1]

Hence elder people have more incident rates, compared to young people. In our study, the people who are at the age of 51-60 years had a high proportion of OA 73.20 (n=142). Followed by people who are aged between 61-70, which occupies 17.53% (n=34) of the total sample size. People who are aged between 71-80, occupies 8.25% (n=16) of the total sample size. People aged between 81-90 occupies 1.03% (n=2) of the total sample size.

By comparing the results in all follow ups based on the pain score (Figure 8), we can see that the pain score of the subjects is reducing.

From our data, the proportion of OA in males was 42.27% (n=82) and the proportion of OA in females was 57.73% (n=112). Hence the largest proportion of patients were found to be as females 57.73% which was following many research studies which says that women are more prone to OA compared to males.[27]

The 188 subjects are admitted to hospital with severe pain and six patients are with moderate pain and no patient was admitted with mild pain. Then the surgeon prescribed glucosamine, diacerein, and methyl-sulfonyl-methane along with supportive medications like analgesics for one month and asked the patients to come for the first follow-up after one month.

In the first follow-up, we measured the pain severity of the patients by using the NPRS and we got the results as 119 patients are in severe pain and 73 patients are in moderate pain and two patients are in mild pain. By comparing the results recorded in first follow-up and on admission, 188 subjects are in severe pain on admission, whereas in first follow-up its count reduced to 119, which is a clear indication that the treatment is showing effect and patient has reduced pain.

On admission six subjects are in moderate pain, then, in first follow-up 73 subjects are in moderate pain, which indicates that the subjects in severe pain category on admission are moved to moderate category because of their reduced pain severity and on admission zero patients are with mild pain, but in followup-1 two patients are in mild pain which indicates that those subjects who are in moderate pain severity on admission have reduced pain severity moved to mild pain severity in first follow-up.

During followup-2, we measured the pain severity of the subjects and got results as, 57 subjects are in severe pain, 131 patients are in moderate pain and six patients are in mild pain. By comparing the results on admission, followup-1 and followup-2, we came to evidence, that the treatment is showing effectiveness and the pain severity of the patients is decreasing. The no. of subjects who experienced severe pain on admission (n=188) have reduced in followup-2 (n=57).

During followup-3, we measured the pain severity of the subjects and we got the results as, 17 subjects are in severe pain, 169 subjects are in moderate pain and eight subjects are in mild pain. By comparing the results we got in all three followup and the results on admission, we concluded that the Glucosamine, Diacerein, and Methyl-sulfonyl-methane are showing effectiveness and reducing pain severity in subjects.

CONCLUSION

In conclusion, following our results, it can be definitively stated that glucosamine, diacerein, and methyl-sulfonyl-methane are effectively treating OA in general, knee OA in particular. We used a NPRS to assess the effectiveness of glucosamine, diacerein, and methyl-sulfonyl-methane in three reviews. The period between any two reviews was one month. On the day of admission, we assessed the pain severity of the subjects by using the NPRS and used X-ray to find the joint space narrowing. Based on the severity, we gave a pain score to the subjects. The same procedure was followed for the next three reviews. In this study, we also found that, after analyzing three reviews, even though the pain was lowering, it doesn't mean that the pain will completely go i.e., the pain score doesn't reach 0 (no pain). The pain was reduced up to a point ex: pain score 2, then it is persisting. Even though we used these medications, the pain is not subsiding. By analyzing the results of all three reviews, we observed, there is a significant decrease in pain severity of the subjects along with symptomatic relief. Based on our study we concluded that glucosamine, diacerein, and methyl-sulfonyl-methane can effectively treat OA by repairing the damaged articular cartilage. But these medications cannot produce new articular cartilage, they only repair the damaged articular cartilage.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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