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ORIGINAL ARTICLE

Effectiveness of Diacerein in Primary Knee Osteoarthritis

MUHAMMAD AMMAR NAQVI[1], OMER IQBAL CHEEMA[2], USMAN LATIF[3], M. SAIF-UR-REHMAN[4], JAHAN ZEB KHAN[5], ZAHID SHAFIQ[6]
[1]*Assistant Professor, Department of Orthopedic Surgery, Sughra Shafi Medical Complex, Narowal.*
[2]*Senior Registrar, Department of Orthopedic Surgery, Services Hospital, Lahore.*
[3]*Senior Registrar, Department of Orthopedic Surgery, DHQ Hospital, Gujranwala.*
[4]*Assistant Professor, Department of Orthopedic Surgery, Sughra Shafi Medical Complex, Narowal.*
[5]*Senior Registrar, Department of Orthopedic Surgery, Jinnah Hospital Lahore,*
[6]*Senior Registrar, Department of Orthopedic Surgery, Services Hospital, Lahore.*
Corresponding author: Muhammad Ammar Naqvi, Email: mammarnaqvi@gmail.com, Cell: 03334251315

ABSTRACT

Objective: To determine role of diacerein among the patient with primary knee osteoarthritis (KOA).
Study Design: An observational cohort study.
Place and Duration: Department of orthopedic surgery, Sughra Shafi Medical Complex, Narowal from June 2021 to May 2022.
Materials and Methods: A total of 100 patients of either gender visiting outpatient department with primary KOA aged 50-75 years were enrolled. Patients were assessed as per Western Ontario and McMaster Universities Arthritis Index (WOMAC) and visual analogue scale (VAS). Diacerein was prescribed 100 mg two times a day for a total duration of six months. WOMAC and VAS were noted before and after completion of the 6 months follow up period.
Results: In a total of 100 patients, 56 (56.0%) were female. Mean age was 63.58 ± 6.42 years while mean BMI was 29.46±3.42 kg/m^2. There were 50 (50.0%) patients who belonged to middle socioeconomic status. Grade of KOA was II in 54 (54.0%) patients. Baseline WOMAC score was 45.12±6.68 while baseline VAS was noted to be 6.81±2.76. At the end of the 6-month treatment period, 83 patients completed the treatment span and so were included in the final analysis. It was found that significant reduction in both WOMAC score ($p<0.0001$) and VAS ($p<0.0001$) were found among the studied patients.
Practical Implications: Diacerein seems to be a good option for relief in symptoms against patients suffering with primary knee osteoarthritis but further randomized trials should be conducted to verify the findings of this study.
Conclusion: Diacerein resulted in significant improvement in the mean WOMAC and VAS scores after six months therapy.
Keywords: Diacerein, improvement, Osteoarthritis Knee, VAS, WOMAC

INTRODUCTION

Osteoarthritis is known to be a degenerative joint disease that gradually progresses with increasing age.[1] Osteoarthritis can cause destruction of the joint articular cartilage. In the initial phase, there is softening, sclerosis, subchondral cysts and ultimately osteophytes formation in the joint.[2] Initial symptoms are joint pain, effusion and stiffness. Local data has revealed that around 25% of the rural population is accompanying primary KOA.[3] The incidence of KOA in the developed countries is estimated to be between 18-25% among male population while it reaches between 24-40% among females beyond the age of 50 years.[4]

All parts of the knee can be affected but mostly medial compartment is involved because during walking repeatedly varus movements causes increased stress on medial compartment causing degenerative changes in arthritis patients. Main aims of the treatment are to relieve pain, limit the progression of disease and to minimize functional disability of the patient.[5] Anti-inflammatory drugs and analgesics are very important in treating these patients. Previous researches have shown that interluki-1-beta (IL-1B) plays main role in the joint cartilage destruction, chondrocyte apoptosis, subchondral bone remodeling and joint inflammation. Cytokines produce nitric oxide which also contribute in joint destruction.[6] Previously many drugs were studied for its treatment like nimesulide and glucosamine sulphate, but diacerein is an anthraquinone derivative which inhibit IL-1B.[7] It relives symptoms and decreases progression of the disease. Primary osteoarthritis is a very common disease causing disability among old age population.

The literature shows moderate to high-quality of evidence supporting the use of diacerein among KOA patients. There is a need to assess the effectiveness of diacerein in prospective cohort studies which can guide us about the role of diacerein in KOA. The existing data highlights benefits of diacerein to be small to be clinically significant which warrants further research.[8] There is no gold standard treatment for KOA so far. Usually, structure modifying or disease modifying agents are used in its treatment. According to some studies, diacerein is a structure modifying agent.[9,10] This study was planned to determine role of diacerein among the patient with primary KOA. In this study, we aimed to prospectively evaluate the effectiveness of diacerein among patients of KOA while the findings of this study were thought to add a potential drug to relieve pain as well as improving quality of life during activities of daily living.

METHODOLOGY

Study Design: An observational cohort study.
Place and Duration: Department of orthopedic surgery, Sughra Shafi Medical Complex, Narowal from June 2021 to May 2022.
Sample Selection: Adopting consecutive sampling technique, a total of 100 patients were enrolled. Inclusion criteria were patients of both genders presenting to the outpatient department with primary KOA aged 50-75 years were included. Patients diagnosed with KOA as per American College of Rheumatology (ACR) criteria having grade II,III and IV disease were included. Exclusion criteria were secondary knee osteoarthritis, using heavy dose of steroids for a duration above 1 year, those patients who had intra-articular steroid injection in the previous 3 months or those who had history of trauma involving knee joint in the last 1 year.
Data Collection: Informed consent was taken from all the patients in study group. Approval was taken from the institutional ethical review board (letter number: 46). Patients were evaluated according to Western Ontario and McMaster Universities Arthritis Index (WOMAC) and visual analogue Scale (VAS). Patients were given diacerein 100mg twice daily for 6 months duration.
Data Analysis: Statistical analysis was done using SPSS (version-26). WOMAC and VAS were recorded of study patients initially and after six months follow up and results were compared. Follow ups were advised at monthly intervals. Patients completing 6-months follow up and treatment period were included in the final evaluation. Independent sample t-test was performed to compare the outcomes. P value<0.05 was taken as significant.

RESULTS

In a total of 100 patients, 56 (56.0%) were female. Mean age was 63.58 ± 6.42 years while 48 (48.0%) patients were aged between 61 to 70 years. Mean BMI was 29.46±3.42 kg/m^2 while 57 (57.0%) patients had BMI between 25-29.9 kg/m^2. Area of residence was urban in 61 (61.0%) patients. There were 50 (50.0%) patients who belonged to middle socioeconomic status. Grade of KOA was II in 54 (54.0%) patients. Table-1 is showing baseline characteristics of

all patients. Figure-1 is showing age distribution of the patients. Figure-2 is describing distribution of KOA grades.

Table-1: Baseline characteristics of Patients with Knee Osteoarthritis (n=100)

Baseline Characteristics		Number (%)
Gender	Male	44 (44.0%)
	Female	56 (56.0%)
BMI (kg/m^2)	<25	20 (20.0%)
	25-29.9	57 (57.0%)
	≥30	23 (23.0%)
Area of Residence	Urban	61 (61.0%)
	Rural	39 (39.0%)
Socio-Economic Status	Low	26 (26.0%)
	Middle	50 (50.0%)
	High	24 (24.0%)

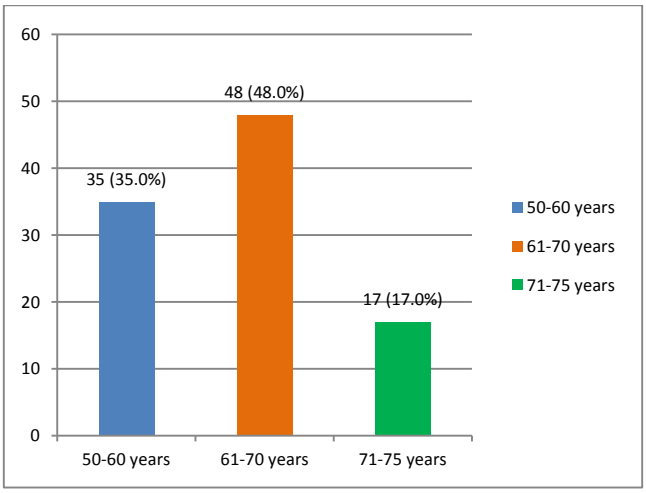

Figure-1: Age distribution of Patients (n=100)

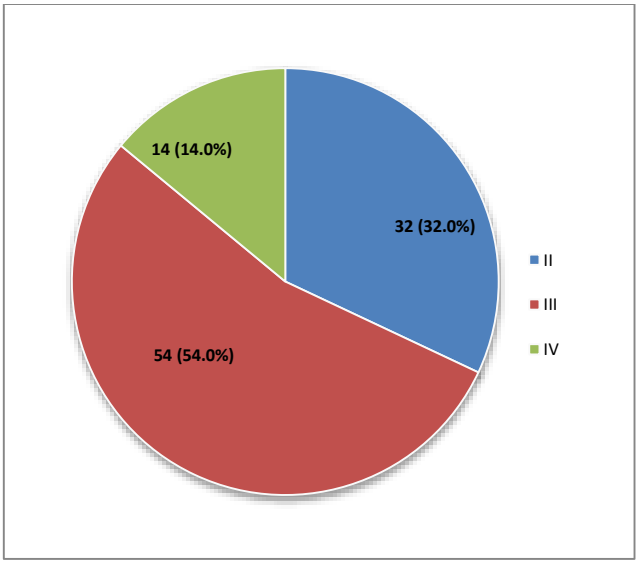

Figure-2: Knee Osteoarthritis Grades (n=100)

Baseline WOMAC score was 45.12±6.68 while baseline VAS was noted to be 6.81±2.76. At the end of the 6-month treatment period, 83 patients completed the treatment span and so were included in the final analysis. Table-2 is showing comparison of WOMAC and VAS scores at the end of the study period and it was found that significant reduction in both WOMAC score (p<0.0001) and VAS (p<0.0001) were found among the studied patients.

Table-2: Comparison of WOMAC and VAS Scores before and after the Diacerein treatment (N=100)

Outcomes	Assessment Interval		P-Value
	Baseline (n=100)	After 6-month treatment (n=83)	
WOMAC Score	45.12±6.68	38.50±9.81	<0.0001
VAS	6.81±2.76	4.34±2.84	<0.0001

DISCUSSION

Osteoarthritis is known to be a debilitating chronic illness that requires long-term treatment especially for the pain and improvement in functional impairments. Diacerein as a structure modifying agent is under practice since many years.[11] This study was conducted to know efficacy of diacerein in primary KOA and improvement in symptoms of patients over the period of six months. Our results were in favor of diacerein with the improvement in mean WOMAC score and VAS after six months therapy. Diacerein is an inhibitor of IL-1B production. Previous literature has shown its role as disease modifying agent.[12,13] A study conducted by Pelletier et al reported significant improvement in KOA after use of diacerein. Their outcomes parameters were radiographic evaluation of the joint.14 In another study by Sharapova et al reported that diacerein showed good outcomes in improving pain and functional disability among patients.[15] Karateev et al conducted study on 100 cases with primary knee osteoarthritis and divided patients in two groups, one group was given conventional treatment and second group given diacerein plus conventional treatment. They concluded that 60% cases receiving diacerein plus conventional treatment showed good outcomes as compared to 20% cases receiving just conventional treatment.[16]

A recent local study conducted by Shahid S et al found that 30% KOA cases showed significant improvement in symptoms and functional disability after six months therapy with diacerein.[17] They used WOMAC score VAS comprising on a question to evaluate functional outcomes in patients. Some other scales like OMERACT-6 and Lequesne Functional Severity Index have also been used in literature, however VAS and WOMAC are simple, reliable and easy to use. Hailer et al in their study reported that diacerein 50mg given two times a day showed very good improvement in VAS and WOMAC score in their patients.[18]

The literature shows that relief in knee pain and maintenance satisfactory joint functions is not always provided among patients of KOA with the utilization of existing set of drugs.[19] With the use of NSAIDs, the chances of gastrointestinal and cardiovascular diseases may increase while other drugs like glucosamine have no obvious benefits.[20] Finding drugs that have anti-inflammatory effects and protect joint function has become an urgent problem in clinical work. Diacerein has been shown to inhibit the production and activity of the cytokine interleukin-1 (IL-1) in vitro and in vivo, thereby protecting cartilage.[21,22]

Absence of comparator or control group was one of the main limitations of this study. Sample was also relatively small. Further randomized controlled trials involving large sets of patients should be conducted to further verify the findings of this study.

CONCLUSION

Diacerein resulted in significant improvement in the mean WOMAC and VAS scores after six months therapy.

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