DIACEREIN: A TREATMENT OPTION IN PAINFUL PRIMARY KNEE OSTEOARTHRITIS

Noreen Akhter, Atif Ahmed Khan, Saeed Bin Ayaz, Syed Mohammad Hassan Akhter*, Aamir Afzal**

Armed Forces Institute of Rehabilitation Medicine Rawalpindi, *Engineering Centre Risalpur,
**College of Physicians and Surgeons Pakistan (CPSP) Islamabad

ABSTRACT

Objective: To identify the efficacy and side effects of Diacerein in patients with mild to moderate knee osteoarthritis.

Study Design: Quasi experimental study.

Place and Duration of Study: Outpatient Department of Armed Forces Institute of Rehabilitation Medicine, Rawalpindi from June 2012 to June 2013.

Material and Methods: Ninety cases fulfilling American College of Rheumatology criteria for diagnosis of Knee Osteoarthritis and falling in Grades I→III of Kellgren-Lawrence Radiological Classification for Knee Osteoarthritis were included. Pre-treatment associated symptoms, complete blood count, renal and liver function tests were documented. After a baseline pain assessment on a 10-Point Visual Analogue Scale, 50 mg of Diacerein was given orally for 4 months followed by pain assessment and inquiry about adverse effects at 6th week, 3rd and 6th months. Post-treatment labs were repeated. Reduction in pain was analyzed by paired-sample t-test using SPSS version 17. Chi-Square test was used to assess the frequency of adverse effects. A *p*-value < 0.05 was considered significant.

Results: Mean age was 61.5 ± 7.8 years. Majority 77 (85.6%) were females. Mean Visual Analogue Scale at start was 6.1 ± 0.87. Significant pain reduction measured on Visual Analogue Scale was observed at six weeks (4.6 ± 1.2) ($p < 0.001$), three months (2.37 ± 0.91) ($p < 0.001$) and six months (2.2 ± 0.85) ($p < 0.001$). Very few patients developed diarrhea 3.3% and nausea 4.4%.

Conclusion: Diacerein is effective drug with minimal side effects for treatment of mild to moderate painful Knee Osteoarthritis

Keywords: American College of Rheumatology criteria, Knee Osteoarthritis (KOA), Kellgren-Lawrence Radiological Classification for Knee Osteoarthritis, Visual Analog Scale (VAS), Diacerein.

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease characterized by fibrillation, thinning and erosion of articular cartilage, depletion of proteoglycan, abnormal replication of chondrocytes and formation of osteophytes at joint margins[1]. Knee Osteoarthritis (KOA) is a common problem in old age affecting 37% of population above 50 years of age[2]. It is estimated that 80% of the population has radiographic evidence of KOA by age 65, although only 60% of those will have symptoms[3]. In the United States, it is the most important cause of physical disability, and a major challenge for healthcare providers[4]. In Pakistan it is the most common cause of locomotor disability[5].

In absence of a curative agent, the main objectives of KOA management are to reduce symptoms, minimize functional disability and limit the progression of structural changes with the ultimate goal of delaying or avoiding arthroplasty. Currently, symptomatic relief in KOA is achieved through analgesics and Non-Steroidal Anti Inflammatory Drugs (NSAIDS) however, their use increases risk of upper gastrointestinal adverse effects and does not affect the underlying pathogenesis of articular diseases. Diacerein or Diacetylrhien is a new oral anti-inflammatory, analgesic and antipyretic drug developed specifically for treatment of OA[6]. It

Correspondence: Dr Atif Ahmed Khan, Armed Forces Institute of Rehabilitation Medicine, Rawalpindi.
Email: dratifkhan02@yahoo.com
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has a novel mode of action that differentiates it from NSAIDs and other conventional forms of drug therapy[7].

The objective of this study was to assess the efficacy and safety of Diacerein in KOA. We used a 10-point Visual Analogue Scale (VAS) score as the outcome measure for quantifying pain.

METHODS

This Quasi-experimental Study was conducted at Outdoor Department of Armed Forces Institute of Rehabilitation Medicine (AFIRM), Rawalpindi from june 2012 to june 2013. Patients who were eligible for study were both male and female of age >50 years with primary KOA fulfilling American College of Rheumatology[8] criteria for diagnosis of KOA and fitting in Grades I, II or III of Kellgren and Lawrence Radiological Classification[9] of KOA.

The exclusion criteria were secondary OA, Grade IV of Kellgren and Lawrence Radiological Classification, intra-articular injection of corticosteroids within last three months or Hyaluronic Acid within last six months, oral treatment with Chondroitin Sulfate, Glucosamine or Diacerein within six months prior to study, primary painful inflammatory or neoplastic conditions of knee, knee surgery planned in next six months, persistent diarrhea or nausea and impaired renal or hepatic functions at the commencement of study. A total of 90 cases were recruited through non-probability purposive sampling. Approval from ethical review committee was taken and all patients signed written informed consent.

Before entering the trial, patients underwent wash out period of 07 days for NSAIDs and 24 hours for other analgesics. The baseline VAS score was recorded. All patients were started oral Diacerein in a dose of 50 mg twice daily for four months. Patients were followed up regularly in the Outdoor Department for at least six months. Progress in pain intensity was assessed by VAS at sixth week, third month and sixth month subsequently.

Complete blood count, renal and liver function tests were carried out at day one and at end of treatment period. All adverse events reported by the patients at study visits were recorded.

Table-1: Comparison of VAS at different times (n = 90).

Time Intervals	VAS	*p*-value*
Baseline	6.11 ± 0.83	-
After 6 weeks	4.6 ± 1.02	< 0.001
After 3 months	2.38 ± 0.92	< 0.001
After 6 months	2.20 ± 0.85	< 0.001

*$p < 0.05$ was taken as levelof significance.

Data had been analyzed with the help of statistical program SPSS version 17. Means and standard deviation were calculated for age and VAS scores before treatment, and at sixth week, third and sixth month post-treatment. Frequencies were calculated for gender and different adverse effects. Reduction in pain was analyzed by paired-sample t-test / Wilcoxon signed ranks test where appropriate. A p-value < 0.05 was considered significant.

RESULTS

A total of 90 patients were included with mean age of 61.5 ± 3.85 years. 13 (14.4%) patients were male and 77 (85.6%) were female. The mean VAS Score before treatment was 6.11 ± 0.83. as compared to baseline VAS score, significant reduction in pain was observed aftert six weeks (p <0.001), after three months (p < 0.001) and after six months (p < 0.001) (Table-1, Fig-1). Only 7 (7.8%) patients experienced minor side effects. Three (3.3%) patients reported diarrhea and 4 (4.4%) patients reported nausea.

DISCUSSION

KOA is likely to become the fourth important cause of disability in women and eighth important cause of disability in men globally; according to a recent World Health Organisation report[2]. In near past, there has been a surge in the use of chondroprotective and connective tissue modifying agents such as chemically modified Tetracyclines, Glucosamine, Chondritin Sulphate and Diacerein[10,11] Consistent beneficial effect of Diacerein has been identified in seven different studies involving 2069 participants. When compared to placebo, pain on VAS was evaluated in 1228 participants and showed a statistically significant reduction in score[12,13]. Our study has also shown significant difference in pain scores based on VAS.

Diacerein is a slow acting drug whose effects become apparent 2-4 weeks after start of treatment, achieving significant level at 4-6 weeks and persist for several months after cessation[13,14]. In our study significant difference was found in pain score at 6 months of the start of treatment (2 months post completion of treatment) with a pain score improved from 6.1 to 2.2. This pain score at 2 months post completion of treatment shows that Diacerein has a long carryover effect.

Diacerein is well tolerated. The predominant adverse effect being transient change in bowel habits[15]. In a study conducted on four groups of participants, the main adverse effect was mild to moderate diarrhea, which occurred in 28.3% of the patients, the magnitude being dependent on the dose of Diacerein[14]. In another study conducted on 1089 participants, 459 (42%) participants were affected initially by diarrhea[13]. Gastrointestinal bleeding, renal, liver or hematological toxicities and allergic reaction have never been reported[13,16]. Few patients in our study experienced diarrhea (3.3%) and nausea (4.4%).

This was the first study in Pakistan to observe the efficacy and the related adverse effects of Diacerein in KOA. However, it was limited by a smaller sample and unavailability of demographic variable comparison. Larger studies are required to confirm the short and long term effectiveness and toxicity of Diacerein therapy in KOA among our own population.

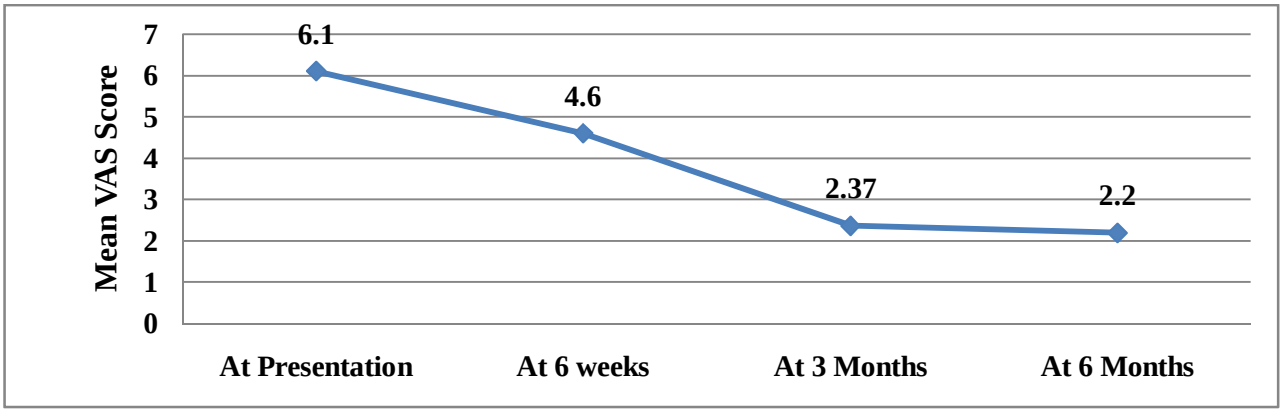

Figure-1: Progression of mean pain score on visual analogue scale.

CONCLUSION

Diacerein is an effective drug for treatment of pain in mild to moderate KOA that has a long carryover effect and few side effects.

Conflict of Interest

This study has no conflict of interest to declare by any author.

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