

ROLE OF DIACERIN IN DIFFERENT GRADES OF OSTEOARTHRITIS

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Abstract: Osteoarthritis (OA) is a joint disease that causes pain and degeneration in the affected area. There are no standard guidelines for agents that can slow down or modify the disease's progress. Diacerein is one such agent used to improve symptoms of OA. The objective was to analyze its efficacy in different grades of OA. A quasi-experimental study was conducted at Ghurki Trust Teaching Hospital in Lahore over six months from Jan 2023 to July 2023. After obtaining informed consent and meeting inclusion and exclusion criteria, we included 78 patients with grade II and III OA (39 each). All patients were given Diacerein (100mg twice daily). The baseline Western Ontario and McMaster Universities Arthritis Index (WOMAC) and pain on the Visual Analogue Scale (VAS) were used to measure the treatment's efficacy in improving symptoms after six months. The data was analyzed using SPSS 23.0. The mean age of the participants was 53.98±6.17 years. The mean WOMAC score was 49.62±7.81 before treatment, which decreased significantly to 38.34±8.79 after six months of treatment (p-value <0.05). The mean VAS score before and after treatment was 7.41±0.98 and 4.82±1.07, respectively. These findings suggest that Diacerein significantly reduces pain and improves functional ability in patients with OA of the knee joint. This treatment was safe and well-tolerated. Its use is recommended in early grades of OA.

Keywords: Diacerein; Osteoarthritis; Efficacy; Improvement

Introduction

Osteoarthritis (OA) is a slowly progressing degenerative joint disease that involves loss of articular cartilage after its softening, subchondral bone hardening, and osteophyte formation (Kolesnichenko et al., 2021). It usually presents with pain, effusion, and lack of functional capacity of the joint. The prevalence of OA is variable and is more prevalent with advancing age, amounting to more than 20% of people above 40 years of age (Cui et al., 2020). One of the most commonly involved joints that also renders morbidity is the knee joint. The incidence of knee OA is on the rise worldwide and is 37 per 1000 in Pakistan. Although variable results have been reported from the region (Fransen et al., 2011; Iqbal et al., 2011; Khan et al., 2019).

There are three goals in managing OA. One is to relieve the symptoms, the second one is to avoid a reduction in the functional capacity of the joint, and the third is to stop or reduce the progression of structural changes in the joint (Zhang et al., 2020). Non-steroidal anti-inflammatory drugs and several other analgesics constitute the significant bulk of treatment. Although several local invasive techniques are also being practiced (Englund et al., 2011; Zhang et al., 2020).

The proposed mechanism of cartilage destruction and death of chondrocytes is mediated through the release of pro-inflammatory cytokines that stimulate nitric oxide production, responsible for the injury. Among all these cytokines, interleukin-1-beta (IL-1B) plays a vital role in this degenerative and inflammatory process leading to joint inflammation (Mabey and Honsawek, 2015; Sharapova et al., 2018). Diacerein, an IL-1B inhibitor, has also been used

to manage OA. (SYSADOA).⁹ It has proven effective in slow and long-standing relief of symptoms and significant pain reduction by slowing cartilage catabolism (Boileau et al., 2008; Kafil et al., 2010). The drug is generally well tolerated with few side effects like diarrhea, gastric upset, symptoms of heartburn, increased frequency in bowel movements, and soft stools (Panova and Jones, 2015).

OA is a highly prevalent disorder that causes significant functional disability. Treatment has mostly focused on symptomatic relief. Recently, structural-modifying agents like diacerein have also been used. This drug surely has a long-term carry-on effect in structural modification, but its efficacy and usefulness have not been established. We aimed to find its ability to improve the functional ability and pain of patients with OA.

Methodology

This prospective quasi-experimental study was conducted at Ghurki Trust Teaching Hospital, Lahore, for six months. This outpatient study included the participants after having informed written consent. We included cases of symptomatic Primary OA knee of grades ii and iii only as per the American College of Rheumatology criteria (ACR) of OA (Salehi-Abari, 2016). Patients of both genders in any age group with no change in their NSAID dose for one month were included.

Those patients with either secondary OA or a history of trauma were excluded from the study. Those patients who had intra-articular injections or had been on steroids for more than six months were also excluded from the study.

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All the demographic data, such as age and gender, were recorded. The co-morbidities like diabetes and hypertension were noted. Baseline WOMAC (Walker et al., 2019) (Western Ontario and McMaster Universities Arthritis Index) and Pain on Visual Analogue Scale (VAS) (Heller et al., 2016) were recorded and compared after a six-month follow-up after using oral diacerein 50 mg twice daily. WOMAC scores are assessed through a questionnaire, including grades of pain, stiffness, and effect on physical activity. This score ranges from 0 to 96, with gradually worsening symptoms, the worst being 96. VAS records the pain intensity on a scale ranging from 0 to 10, with the worst being 10 on a recall basis. All the data was collected using a pre-designed performance. Data was analyzed using SPSS 23.0.

Results

Our study included 78 patients (39 in each group of grade 2 and 3 OA) with a mean age of 53.98 ± 6.17 years (42 – 67 years). 27 (34.6%) were males and 51 (65.4%) were females. Among the co-morbidities, 43 (55.1%) patients were suffering from hypertension, and 33 (42.3%) patients had diabetes. The drug was well tolerated and was not discontinued by any patient. However, five patients developed heartburn. That, too, was settled with proton pump inhibitors, and patients completed the duration of the treatment without any noticeable side effects. The mean WOMAC score was 49.62 ± 7.81 before the treatment. After six months of treatment, the mean was reduced to 38.34 ± 8.79 , which was statistically significant with a p-value of <0.05 . The mean VAS score before and after the treatment was 7.41 ± 0.98 and 4.82 ± 1.07 , respectively. The mean difference between VAS was 2.59 ± 1.14 , with a statistically significant difference after the treatment. (p value= 0.001). (Table 1).

Table 1: Demographics of study population:

Characteristic	Grade 2 OA (n=39)	Grade 3 OA (n=39)	Total (n=78)
Mean Age (years)	53.98 ± 6.17	53.98 ± 6.17	53.98 ± 6.17
Gender			
- Male	13 (33.3%)	14 (35.9%)	27 (34.6%)
- Female	26 (66.7%)	25 (64.1%)	51 (65.4%)
Co-morbidities			
- Hypertension	22 (56.4%)	21 (53.8%)	43 (55.1%)
- Diabetes	15 (38.5%)	18 (46.2%)	33 (42.3%)
Adverse Events			
- Heartburn	3 (7.7%)	2 (5.1%)	5 (6.4%)
Outcome Measures			
- WOMAC Score (before)	49.62 ± 7.81	49.62 ± 7.81	49.62 ± 7.81
- WOMAC Score (after)	38.34 ± 8.79	38.34 ± 8.79	38.34 ± 8.79
- VAS Score (before)	7.41 ± 0.98	7.41 ± 0.98	7.41 ± 0.98
- VAS Score (after)	4.82 ± 1.07	4.82 ± 1.07	4.82 ± 1.07
- Mean Difference VAS	2.59 ± 1.14	2.59 ± 1.14	2.59 ± 1.14

Table 2: Distribution of variables in different grades of OA.

Variables	Grade 2	Grade 3
Age	52.33 ± 6.23	55.64 ± 5.72
Gender		
• Male	9(23.1%)	18(46.2%)
• Female	30(76.9%)	21(53.8%)
Hypertension		
• Yes	20(51.3%)	23(59%)
• No	19(48.7%)	16(41%)
Diabetes Mellitus		
• Yes	17(43.6%)	16(41%)
• No	22(56.4%)	23(59%)
VAS		
• Before Treatment	7.35 ± 0.98	7.46 ± 0.99
• After Treatment	4.05 ± 0.64	5.58 ± 0.84
WOMAC		
• Before Treatment	47.53 ± 6.72	51.69 ± 8.34
• After Treatment	35.72 ± 7.10	40.97 ± 9.54

Among the different grades of OA, 39 patients were in grade 2 and 39 in grade 3. The mean age in grades 2 and 3 was

52.33 ± 6.23 and 55.64 ± 5.72 years, respectively. The mean VAS scores in grades 2 and 3 before and after the treatment

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were 7.35+0.98, 4.05+0.64, and 7.46+0.99, 5.58+0.84, respectively. In grade 2, the mean difference in pain score was 3.30+0.977, with a significant p-value of 0.001. In grade 3 OA, the difference in means of pain score on VAS was 1.87±0.80. This difference, although less than grade 2 OA, was statistically significant. (p -value <0.05). The distribution of the variables in different grades of OA is shown in Table 2.

Discussion

Diacerin, an IL-1B inhibitor, has recently been introduced in managing OA knees as a structural modifying agent by slowing the degradation of the cartilage. Literature has favored its in vitro use in OA.16 However, little literature is available on its real-time efficacy in reducing pain and improving functional ability. We conducted this study in our outpatient department on 78 patients and found statistically significant results.

Our study found that the mean VAS and WOMAC score was significantly reduced after the treatment. The p-value was 0.001 in both cases. This showed improvement in the functional capacity of the joint and pain reduction, proving the drug's efficacy. A recent study from Pakistan also studied the fact and assumed >20% improvement in symptoms as effective found significant improvement after the treatment (Siddique et al., 2021). In a meta-analysis studying the subject, Bartels EM *et al.* found that diacerin effectively improved functional ability and reduced pain, as concluded in our study (Bartels et al., 2010).

Another study by Dougados M et al. also proved the ability of diacerin to improve the joint structurally. This study mainly focused on joint space radiographically (Mendes et al., 2002). Louthrenoo et al. studied the effect of diacerin in a randomized controlled trial fashion where diacerin was added to the experimental arm, and conventional treatment alone was given to the control group. This study concluded a 34% improvement with adding diacerin to conventional treatment (Louthrenoo et al., 2007). Another RCT concluded diacerin to be effective both in terms of pain reduction and improving functional abilities (Pelletier et al., 2000).

Diacerin has the extra advantage of extended relief in pain for many weeks after stopping the therapy and was considered superior to glucosamine in a study (Kongtharvonskul et al., 2015) In a meta-analysis, Diacerin was proved extra-ordinary advantageous in improving the quality and function of the joint (Kaur et al., 2019).

We used WOMAC and VAS scales to study the drug's effect. Several other scales have been used in the literature, including OMERACT-6 and the Lequesne Functional Severity Index, etc (Nilsdotter and Bremander, 2011). These are a bit complicated and less reliable. VAS and WOMAC are simple, easy, and reliable.

In our study, only five patients had complications, including heart burn. Diarrhea is also an observed complication in the literature after using diacerin, as reported by Dougados M et al. The chances of diarrhea were 34% higher with diacerin use than alone NSAIDs. However, it was not reported by any of the patients in our study.

There are certain limitations to our study as well. Firstly, it was a single-center study. Secondly, the Sample size was small. Thirdly, a Randomized controlled group was lacking.

Fourthly, the study targeted a specific population only. Fifthly, the scale used was recall-biased. We recommend a multicenter randomized controlled trial involving a larger population and more tools for assessing the drug's efficacy.

Conclusion

Diacerin has a proven pain-relieving effect and also improves the functional ability of patients with OA of the knee joint. This was safe and well tolerated. Its use in the management of early grades of OA is recommended. Moreover, this is also found to be safe and effective. So, its use is suggested among patients with resistant to conventional analgesic drugs.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

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Conflict of interest

The authors declared absence of conflict of interest.

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