Original Article

Effectiveness Of Diacerein In Treatment Of Knee Osteoarthritis

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Doi: 10.47750/pnr.2022.13. S05.111

Abstract

Background: Osteoarthritis (OA) is a common joint disorder. Oal non-steroidal anti- inflammatory drugs (NSAIDs), including selective cyclooxygenase-2 (COX-2) inhibitors, are the mainstay of pharmacotherapy but it can not be used for long time due to their adverse effects. Diacerein is SYSADOAs, an advantage of using diacerein in OA treatment is, that Diacerein does not affect the synthesis of prostaglandins, and does thereby not have a deleterious effect on the upper gastro-intestinal mucosa. This is an important advantage compared to NSAID treatment. But still there is still no consensus on the place of Diacerein in OA because there is lack of pragmatic trials those have evaluated the effectiveness of Diacerein in real life situations.

Objective: So this study was planned to evaluate the effectiveness of Diacerein in symptomatic treatment of knee OA.

Methods: All the Patients were given Diacerein 50 mg BD. The evaluation of effectiveness will be in terms of improvements in symptoms and physical functions of patients.

Results: Diacerein is not as effective in controlling clinical symptoms of knee Osteoarthritis as it claimed to be. It also takes long time to show a clinically relevant & appreciable effect.

Conclusion: Diacerein is a overrated drug in Osteoarthritis which is mainly due to lack of pragmatic trials of this drug. Pragmatic clinical trials should must be done to know the real place of a drug in management of any condition

Keywords: Osteoarthritis, NSAID,SYSADOA, ESCEO,WOMAC, NSAID

INTRODUCTION

Osteoarthritis (OA) is a common joint disorder and may occur in any synovial joint in the body, although the condition is most common in knee joint in Indian population. The pharmacological management of OA is mainly symptomatic [1]. Paracetamol is the first-line oral analgesic, whilst oral non-steroidal anti- inflammatory drugs (NSAIDs), including selective cyclooxygenase-2 (COX-2) inhibitors, are the mainstay of therapy[2,3] , but NSAIDs and paracetamol are known to cause potentially severe hepatic, gastrointestinal, renal, cutaneous and cardiovascular reactions, so these drug cannot be used for long time. Therefore, there remains a need for a therapeutic agent for OA that has symptom-modifying effects and a better safety profile[6]. Diacerein was introduced to fill this gap . An advantage of using diacerein in OA treatment is, that Diacerein does not affect the synthesis of prostaglandins ,and does thereby not have a deleterious effect on the upper gastro-intestinal mucosa which is an important advantage compared to NSAID treatment. [4] But still there is no consensus on the place of SYSADOAs in general but Based on a literature review of clinical trials and meta-analyses, the ESCEO confirms that the efficacy of Diacerein is similar to that of non-steroidal anti-inflammatory drugs (NSAIDs) , and superior to that of paracetamol after the first month of treatment.[5] Although there are many explanatory trials which have evaluated the efficacy of Diacerein in OA knee but still there is lack of pragmatic trials those have evaluated the effectiveness of Diacerein in real life situations. So this study was planned to know the effectiveness of Diacerein in real life setting to evaluate effectiveness of Diacerin in releaving symptoms and improving physical functions of patients with knee osteoarthritis.

MATERIAL AND METHODS:

This is a prospective, open label, 120 days clinical study. Diacerein is an anthraquinone derivative of which the active metabolite is rhein. It was developed for the treatment of osteoarthritis. It works by blocking the action of interleukin-1 beta, a protein involved in the inflammation and destruction of cartilage that play a role in the development of symptoms of osteoarthritis [7].

Sample size was of 80 patients which was calculated by using the statistical program Nnpar (IDV.

Inclusion Criteria

- Patients of all genders and all age groups having Symptomatic osteoarthritis of knee.
- Females of child bearing potential must have a negative pregnancy test result.

Exclusion criteria

- Patients who had received systemic coriticosteroids within 4 weeks or intra-articular glucocorticoids within the preceding 3 months.
- Painful knee conditions other than OA.
- NSAIDs or paracetamol within 3 days prior to enrollment .
- Opioid analgesics use within 7 days prior to enrollment.
- Patients bound to wheel chair or bed and unable to carry out self-care activities.
- Inability to comply to study procedures.

Study Procedure

Patients attending orthopaedics OPD with knee osteoarthritis was included in the study using inclusion/exclusion criteria and after taking written and informed consent. All the Patients were given Diacerein 50 mg BD. The evaluation of effectiveness will be in terms of improvements in symptoms and physical functions of patients. Each patient will be evaluated for pain, stiffness and physical functions by using 100 mm visual Analog format of western Ontario and Mc Master University Osteoarthritis index at the baseline (Day-0), Day-7,Day-15 Day-30,Day-60,Day-90 and Day-120.

Statistical Analysis:

Statistical analyses were performed using SAS software.

RESULTS:

A total of 210 patients were screened from which 80 patients had been assigned the treatment. 9 patients failed to complete the study in which 3 were due to adverse events, 4 due to lack of effectiveness and 2 due to unknown reasons (just lost to follow up). 56.25% patients were female while mean ± SD age was 65.23 ± 8.51 years and the mean ± SD BMI was 28.12 ± 2.00 Kg\m2.

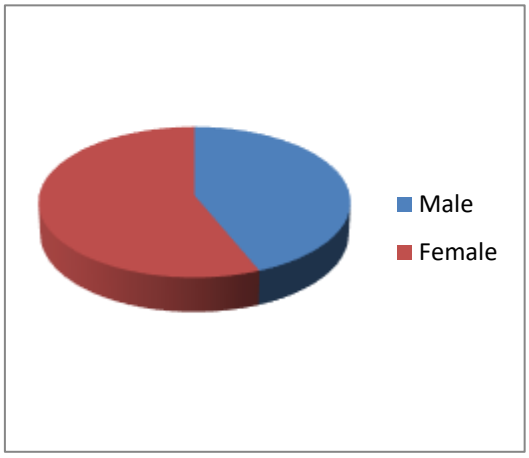

Fig-1 Gender Ratio

Effectivenss

Baseline mean ± SD of WOMAC pain, WOMAC stiffness & WOMAC physical function scores were 315.05 ± 47.87, 122.81 ± 14.61 & 1071.68 ± 163.37 respectively. After 7 days Diacerein treated patients exhibited 0.69% (P<0.0001),0.17% (P<0.0001) and 0.26% (P=0.0200) reduction in reductions in WOMAC pain , WOMAC stiffness and WOMAC physical function scores respectively ,compared with the corresponding baseline scores .

After 15 days it exhibited 1.42% (P<0.0001), 0.46%(P<0.0001) and 0.64% (P<0.0001) reduction in the same respectively when compared with the corresponding baseline scores .

After 30 days the same exhibited 14.62%(P<0.0001),8.59%(P<0.0001) and 15.49%(P<0.0001) reduction in reductions in WOMAC pain , WOMAC stiffness and WOMAC physical function scores respectively ,compared with the corresponding baseline scores .

After 60 days the same exhibited 29.51%(P<0.0001), 20.25%(P<0.00010) and 23.51%(P<0.0001) reduction in WOMAC pain , WOMAC stiffness and WOMAC physical function scores respectively ,compared with the corresponding baseline scores.
After 90 days the same exhibited 38.79 % (P<0.0001), 26.14% (P<0.0001) and 29.91 %(P<0.0001) reduction in WOMAC pain , WOMAC stiffness and WOMAC physical function scores respectively ,compared with the corresponding baseline scores.
After 120 days the same exhibited 41.88% (P<0.0001), 32.19(P<0.0001) and 35.24% (P<0.0001)) reductions in WOMAC pain , WOMAC stiffness and WOMAC physical function scores respectively ,compared with the corresponding baseline scores .

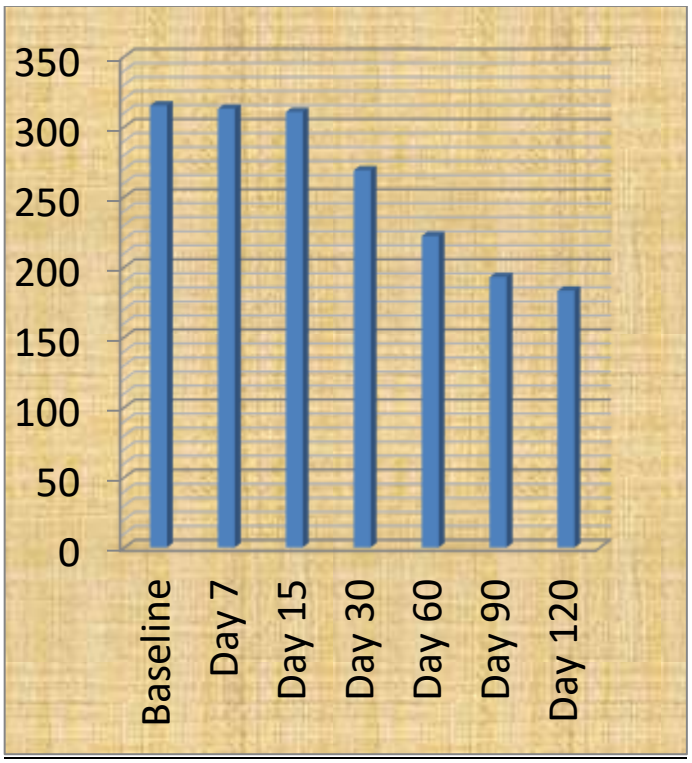

Fig-2 WOMAC Pain Score

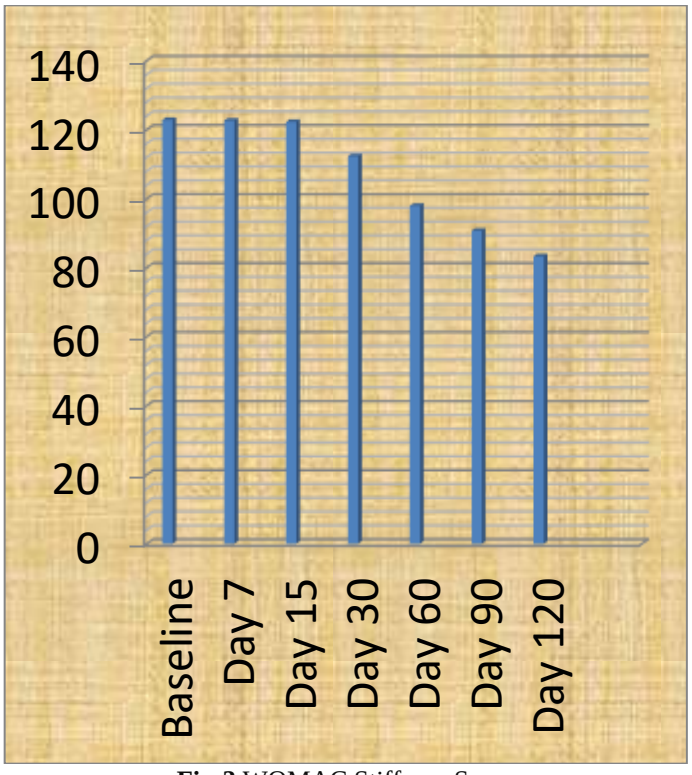

Fig-3 WOMAC Stiffness Score

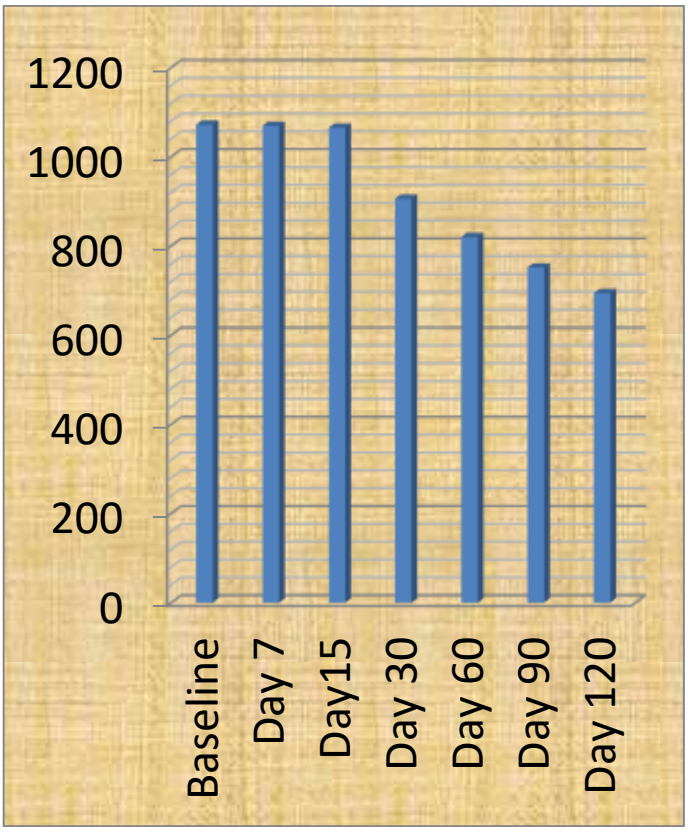

Fig-4 WOMAC Physical Function Score

DISCUSSION:

After 7 days Diacerein treated patients exhibited 0.69% ,0.17% and 0.26% reduction in the WOMAC pain , WOMAC stiffness and WOMAC physical function scores respectively when compared with the corresponding baseline scores while after 15 days Diacerein treated patients exhibited 1.42%, 0.46% and 0.64% reduction in the same respectively when compared with the corresponding baseline scores which is hardly relevant clinically . This is in line with the meta-analysis done by Bernhard Rintelen et al (2006) .

After 30 days the same exhibited 14.62%, 8.59% and 15.49% reduction in the same respectively when compared with the corresponding baseline scores but this is not in accordance with the study done by Karel Pavelka et al (2007) in which 52%,52.5% &52.11% reduction in pain , stiffness and physical function scores respectively was seen ,compared with the corresponding baseline scores. This is also not accordance with study done by W. Louthrenooet al (2007) in which 32.85 %,30.99% & 27.66 % reduction in the same respectively was seen . The above huge difference in the drug effect is appear to be due to non pragmatic nature of the above studies while we had a pragmatic study .This phenomenon is potentiated by the study done by Navin Gupta et al (2012) which was a pragmatic study of a small sample size in this study 13.17%,12.32% & 13.6% reduction in WOMAC pain , WOMAC stiffness and WOMAC physical function scores respectively was seen compared with the corresponding baseline scores which is in line with our study. So it is clear that in real life situation effectiveness of Diacerein is surprisingly less than the efficacy observed in the studies which are not done in real life situation.

After 60 days the same exhibited 29.51%, 20.25% and 23.51% reduction in the same respectively when compared with the corresponding baseline scores. The later is not supported by W. Louthrenoo et al (2007) study in which 51.39%,47.01%,43.76% reduction in same parameters respectively were seen while it is supported by Navin Gupta study et al(2012) which was done in real life situation while previous was not . So it is clear that in real life situation Diacerein is not much effective .

After 90 days Diacerein treated group exhibited 38.79 % ($P<0.0001$),26.14% ($P<0.0001$) and 29.91 %($P<0.0001$) reduction in the same respectively when compared with the corresponding baseline scores and it is not supported by the study of W.Louthrenoo et al (2007) which is of non pragmatic nature in which 64.11%, 61.29%,59.34% reduction in the above scores were seen .

After 120 days the same exhibited 41.88% , 32.19 and 35.24% reduction in the same respectively. This is not accordance with the study of W.Louthrenoo et al (2007) which was a non pragmatic study and 70.21, 65.80% and 66.70% in the same was observed.

CONCLUSION

Diacerein is not as effective in controlling clinical symptoms of knee Osteoarthritis as it claimed to be. It also takes long time to show a clinically relevant & appreciable effect and due to it there are always chances of non adherence to

treatment. Diacerein is a overrated drug in Osteoarthritis which is mainly due to lack of pragmatic trials of this drug. Pragmatic clinical trials should must be done to know the real place of a drug in management of any condition.

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