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Assessment of Pain by the Performance on the Visual Analogue Scale (VAS) In Patients Treated With Celecoxib and Diclofenac in Osteoarthritis of Knee Joint: A Follow up Study

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ABSTRACT

Osteoarthritis is a joint inflammation that results from cartilage degeneration in which nonsteroidal antiinflammatory drugs (NSAIDs) are the commonly used analgesics. This study intended to compare the selective NSAID (celecoxib) and non specific NSAID (diclofenac) in terms of Visual Analog Scale (VAS) scoring.This was a 7 days follow up study. Fifty male patients attending the out patient department of orthopedics with diagnosed osteoarthritis of knee joint were chosen. Patients treated with celecoxib were cosidered as group 1 and patients treated with diclofenac as group 2. VAS scoring was obtained before the treatment (day 1) and after the treatment (day 3, 5 and 7). Responses were analyzed using Paired Wilcoxon signed rank test and the rates of adverse events were compared between the two treatment groups using the Fisher's exact test. The patients were aged between 40 to 60 years. The age difference was not statistically significant (p-value = 0.59). The VAS scores between the groups before the treatment were not statistically significant. After the treatment, comparison for the corresponding days (i.e. day 3, 5 and day 7) showed that the difference in VAS scores were statistically significant only on day 5 and 7 ($p<0.001$). The comparison of the GI adverse events showed the difference was statistically significant ($p<0.01$). Also, the cost incurred on PIP was more with the patients treated with diclofenac. Celecoxib was associated with a lower VAS pain score and less upper gastrointestinal symptoms when compared to diclofenac in osteoarthritis of the knee joint.

Keywords: Osteoarthitis, Celecoxib, Diclofenac, NSAID

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INTRODUCTION

Osteoarthritis is a joint inflammation that results from cartilage degeneration. It is often associated with joint pain, tenderness, stiffness, locking, and sometimes an effusion leading to disability and impaired quality of life. [1] Prostaglandins are the contributors for the development of signs and symtoms seen in osteoarthritis. Cyclooxygenases are the enzymes invoved in the production of prostaglandins. [2] Inhibition of these enzymes reduces the inflammation and its accompanying pain, fever, swelling and tenderness. Diclofenac and Celecoxib are the nonsteroidal antiinflammatory drugs (NSAIDs) that are commonly used drugs which inhibit cyclooxygenases to reduce proataglandin synthesis and consequently the joint pain and inflammation. [3]

Though Diclofenac is a popularly used drug, its exact mechanism of action is not entirely known but the primary mechanism responsible for its action is thought to be inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX) and hence non specific. [4] Celecoxib is specific inhibitor of enzyme COX-2. Probably because of this celecoxib differs from diclofenac in that it causes less inflammation and ulceration of the stomach. [5] Therefore, this study intended to find the presence of compromise on pain if present with the celecoxib because of its selective action. Also, dIclofenac is comparitively cheaper than celecoxib; hence we also intended to compare the cost-effectiveness between diclofenac and celecoxib.
Visual Analog Scale (VAS) is a commonly used tool to quantify pain in clinical investigation. It is based on the subjective experience of pain. [6] Therefore, this study employed VAS to determine its severity and adequacy of its relief before and after the treatment with celecoxib and diclofenac.

MATERIALS AND METHODS

This was a 7 days follow up study conducted at department of pharmacology, Sri Siddartha medical college (SSMC), Tumkur, after the approval of the research and ethical committee. Fifty male patients attending the out patient department of orthopedics with diagnosed unilateral osteoarthritis of knee joint were chosen. The study details and Visual Analog Scale (VAS) were explained to the participants and a written consent was obtained. Since gender differences exist in occurance of osteoarthritis of the knee, only male patients were selected for this study to avoid gender bias. [7] Care was taken to avoid significant differences in demographic characteristics of the patients.

The VAS consisted of a hundred millimeter line on an A4 paper. It contain reading from 0 to 10, where 0 indicated ‘No pain at all’ which is printed on the extreme left of the line and 10 indicated ‘severe uncontrollable’ pain on the right. VAS was tested on the day of the patients’ visit to hospital i.e. before the administering the drugs and a copy of VAS was also provided to each patient. The patients were randomized to receive celecoxib or diclofenac. Twenty five patients were treated with celecoxib 200 mg and 25 patients with diclofenac 75 mg once day for 7 days. The day of visit of the patient was considered as the day 1 and medication was

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instituted from the day 1. The patients were provided with 3 VAS sheets and were instructed to rate the pain on day 3, 5 and on day 7 and requested them to report on the 7th day and submit the VAS sheets. Patients were also followed up telephonically on day 3, 5 and on day 7. The phone calls were made at 11 AM and are requested to rate their pain perception on VAS provided to them. Gastrointestinal (GI) adverse events were documented throughout the study and were treated with proton pump inhibitors (PIP).

Patients treated with celecoxib were cosidered as group 1 and patients treated with diclofenac as group 2. Quantitative data of the 2 groups were summarized to test the difference in mean of the VAS scores. Two types of comparisions were performed. First, comparision was made between the groups for the corresponding days. Second, in each group comparison was made between the VAS scores of the 3 days. Responses were analyzed using Paired Wilcoxon signed rank test with 95% confidence intervals. The rates of adverse events were compared between the two treatment groups using the Fisher's exact test.

RESULTS

The patients were aged between 40 to 60 years. Mean age of the group 1 (patients treated with celecoxib) was 49.88±5.74 and mean age of the group 2 (patients treated with diclofenac) was 50.08±5.56. The age difference was not statistically significant (p-value = 0.59). The VAS scores between the groups for the corresponding days (i.e. day 3, 5 and day 7) were compared and shown in table 1 and chart 1. Paired Wilcoxon signed rank test with continuity correction was performed to compare. It showed that the difference in VAS scores were statistically significant only on day 5 and 7 ($p<0.001$). In group 1, five patients had gastrointestinal disturbances and in group 2, fifteen had gastrointestinal disturbances (table 2). These adverse events were compared using Fisher's Exact Test, which showed the difference was statistically significant ($p<0.01$, odds ratio: 0.17). The proportion of cost incurred on PIP was 17.3% and 2% in the patients treated with diclofenac and celecoxib respectively (Table 3).

Table 1: Comparison between the VAS scores for the corresponding days with respect to their treatment with celecoxib and diclofenac

	Group1(Celecoxib)	Group 2 (Diclofenac)	p value*
Day1	8.17 ± 0.56	8.22 ± 0.55	0.68
Day 3	5.67 ± 0.62	5.76 ± 0.63	0.32
Day 5	2.70 ± 0.65	2.95 ± 0.59	<0.001
Day 7	2.08 ± 0.54	2.39 ± 0.53	<0.001

* Wilcoxon signed rank test with continuity correction

Table 2: Comparison of the proportions in each group having adverse events

Drug	No of patients with GI disturbances (n=25)	p value*
Group1(Celecoxib)	5	<0.01
Group 2 (Diclofenac)	15	

*Fisher's Exact Test

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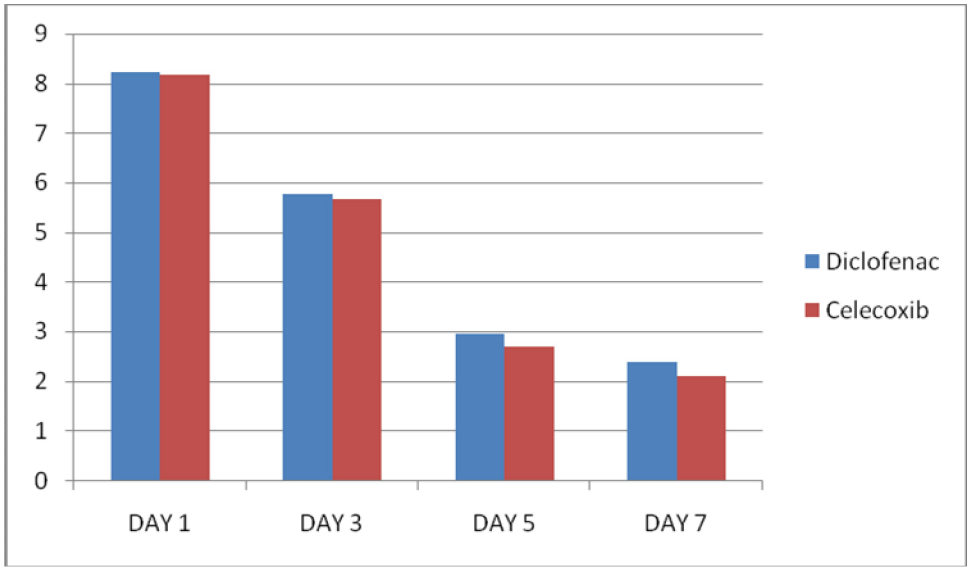
Table 3: Comparison of the total cost incurred on pain management of osteoarthritis of knee joint in rupees between the two groups for 7 days

Drug	Cost on NSAIDs	Cost incurred on PIP	Total cost of the treatment
Group 1 (Celecoxib)	1522.5	45	1567.5
Group 2 (Diclofenac)	787.5	165	952.5

Chart 1: Shows VAS scores for Celecoxib and Diclofenac on day 3, 5 and 7



DISCUSSION

Management of pain in osteoarthritis is one of the challenging tasks in the clinical practice. [8] Concern has arisen in the last few years regarding the potentials of non specific NSAIDs and COX-2 selective inhibitors. [9] Therefore, this study intended to compare the celecoxib and diclofenac as single dose therapy in the treatment of osteoarthritis of the knee joint.

The results of our study demonstrated that clinically relevant improvement was achieved at 7 days in both the treatment groups, as indicated by the reduction in the VAS scores. As a single dose, the efficacy of celecoxib 200 was found to be better than diclofenac 75 mg in terms of VAS scores. The amount of fall in VAS scores was significantly higher in patients treated with celecoxib as suggested by the significant difference in VAS scores on 5^{th} and 7^{th} day of treatment. Treatment was well tolerated with celecoxib exhibiting less frequent gastrointestinal adverse events than diclofenac. The results were in consistent with other studies. [10] Though diclofenac costed less, it was found that treatment with celecoxib was advantage in terms of low VAS scoring, less additional cost on PIP and improved patients'

quality of life. Thus, this study suggests that celecoxib being a selective COX-2 inhibitor does not show any compromise on pain in osteoarthritis of knee joint.

To Conclude, Celecoxib was associated with a lower VAS pain score and less upper gastrointestinal symptoms when compared to diclofenac in osteoarthritis of the knee joint.

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