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A Comparative Study of Lornoxicam and Diclofenac in Patients Suffering from Osteoarthritis.

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Research Article

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ABSTRACT

Lornoxicam is comparatively a newer NSAID. This study was done to compare the efficacy and tolerability of lornoxicam and diclofenac in the treatment of patients suffering from osteoarthritis over 32 weeks. A randomized, open, parallel-group trial of patients with OA of knee enrolled 223 patients. Out of 223 patients enrolled 216 patients participated in the study. The available patients were randomly divided into two groups. One group of 108 patients received lornoxicam 4-8 mg BID. for 32 weeks, another group of 108 patients received diclofenac 50-100 mg TID. for 32 weeks. Assessments were made at baseline, 4 weeks, 8 weeks and then every 10 weeks. They comprised pain score, adverse reactions and withdrawals. The VAS score was reduced in lornoxicam group by 22.51% and 19.16% in diclofenac group. These values were significant from baseline values in both the groups and reduction in lornoxicam group was significant in comparison to diclofenac group. During the next 22 weeks pain intensity continued to decrease but this reduction was not significant. The adverse events were significantly less in the lornoxicam group in comparison to diclofenac group. Lornoxicam 4-8 mg bid was more effective as analgesic in comparison to diclofenac 50-100 mg TID. The lornoxicam was tolerated better than diclofenac. Thus, lornoxicam appears to be a useful therapeutic alternative to diclofenac in patients suffering from osteoarthritis.

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are very commonly used for patients suffering from osteoarthritis (OA) [1,2,3,4,5]. A number of studies have shown that lornoxicam is either equivalent or more efficacious than other NSAIDs [6,7,8]. A study showed that lornoxicam was comparable to diclofenac in effectiveness and tolerability after 4 weeks of treatment in adult Indian patients with O.A. of the hip or knee who completed the study[9]. However there are doubts about their overall efficacy [10,11,12]. Many physicians believe that NSAIDs provide some symptomatic relief in rheumatoid arthritis but do not prevent erosions or alter disease progression [13,14]. Even regarding symptomatic relief it is not sure whether NSAIDs are more efficacious than placebo or not and whether the analgesic effect is long lasting or not. Patients have responded equally even to paracetamol in comparison to NSAIDs [15]. Lornoxicam is a member of the oxicam group of nonsteroidal anti-inflammatory drugs (NSAIDs). Oxicams have potent anti-inflammatory and analgesic effects, but their use is associated with a high risk of gastrointestinal adverse effects. In a study of patients with dorsalgia Lornoxicam proved to be more effective than nimesulide, meloxicam and diclofenac [16]. In addition, oral doses of lornoxicam of 16-24 mg daily have been more effective than tramadol 300 mg daily in pain following knee surgery. Lornoxicam combines the high therapeutic potency of oxicams with an improved gastrointestinal toxicity profile as compared to naproxen, for example. This is probably due to the short half-life of lornoxicam as compared to the other oxicams.

Lornoxicam, a modern oxicam with balanced COX-1/COX-2 inhibition, has been in the market for a long time. Numerous controlled clinical studies have shown the excellent efficacy and tolerability of this agent, and experience from clinical practice has confirmed this.

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A direct comparison between lornoxicam and diclofenac, with respect to efficacy and tolerability was performed in the medicine O.P.D. of our hospital which is a tertiary care centre.

MATERIALS AND METHODS

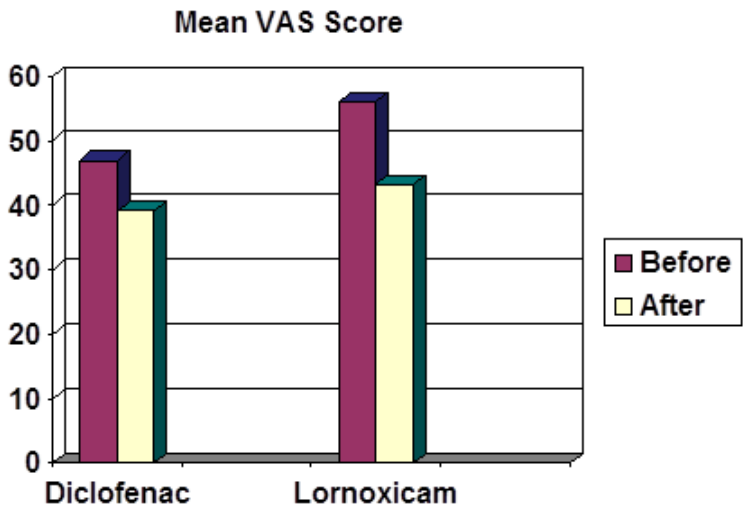
A total of 223 patients with osteoarthritis were enrolled in this trial. 216 patients participated in the study. This 32 week randomized, open, parallel group study was undertaken to compare oral Lornoxicam 4-8 mg b.i.d. and Diclofenac 50-100 mg t.i.d. in patients with OA of the knee. The doses selected are recommended doses for these two drugs. There were 120 females and 96 males, median age 60 years (range 32-80). All had symptomatic and radiological evidence of OA of one or both knee joints. Patients were excluded who had previous dyspeptic problems and/or hypersensitivity with NSAIDs. There were no significant differences in pain at the start of therapy. All patients gave written informed consent for participation. Patients were asked to continue in the study until their treatment arm was stopped or unless they desired. Compliance was determined by counting of returned tablets. Patients returned the study medication at each visit and compliance was 80% for lornoxicam group and 74% for diclofenac group.

Assessments were made at baseline, 4 weeks, 8 weeks and then every 10 weeks. Visual analog scales (VAS), using 100 mm horizontal scales (0 = no pain; 100mm = maximum pain) were used to record overall pain, pain at rest and pain on movement. Adverse effect profile was made on sign and symptom basis. Investigations based on sign and symptoms were made where deemed necessary and the patients were excluded from the study if necessary. The primary endpoints were the VAS score for pain among the patients who completed the study.

RESULTS

In the Diclofenac group the initial mean overall VAS pain score was 47.15 (95% CI 44.72- 49.58) and this had fallen at 4 weeks to37.9 (95% C.I. 35.34-40.46). Mean overall VAS pain score in the Lornoxicam group was initially 55.75 (95% C.I. 53.11-58.38) and this had fallen at 4 weeks to 43.2 (95% C.I. 41.53-44.86)(Fig. 1). Comparison showed a highly significant reduction in overall VAS pain scores with lornoxicam ($p<0.001$) and diclofenac ($p<0.02$). Altogether lornoxicam reduced overall VAS pain scores during the first 4 weeks of treatment by 22.51% and diclofenac by 19.61%. An alternative analysis showed that 43 patients (40%) in lornoxicam group had severe overall pain at baseline which reduced to 15 patients (14%) after 4 weeks; whereas in diclofenac group 49 patients (43%) had severe overall pain at baseline which reduced to 29 patients (28%) after 4 weeks. The $\chi 2$ test showed significant differences between lornoxicam and diclofenac ($P< 0.05$). After 4 weeks there were no further significant differences in overall VAS score from initial values in both the groups.

Figure 1: Bar Diagram Showing VAS Score



Adverse Reactions

44% of patients receiving lornoxicam and 60% 0f patients receiving diclofenac reported adverse effects (Table 1). The number of adverse reactions in diclofenac group was significantly greater in comparison to lornoxicam ($x^2 = 5.068$; d.f. = 1; $p<0.05$).

Gastrointestinal adverse reactions including dyspepsia and nausea, were the commonest side effects, occurring in 33% of patients receiving lornoxicam and 47% of patients receiving diclofenac.

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Urogenital problems were second common adverse events. One patient complained of itching in palms which subsided spontaneously in four days.

Withdrawals

The withdrawal rate was more in diclofenac group. At 32 weeks 89% of patients in lornoxicam group and 74 % of patients in diclofenac group remained on therapy.

Table 1: Percentage of patients showing adverse effects and withdrawals

Drug Group	%age of patients showing adverse effects	%age of patients withdrawn
Diclofenac(n_1)	60	26
Lornoxicam(n_2)	44	11

(n_1=108; n_2=108)

DISCUSSION

Daily dosages of the drugs were on the basis of the individual clinical status in the range of the dose-recommendations in the package-leaflet determined by the physicians. More patients in the lornoxicam group were treated with half of the doses i.e. 4 mg (30%) than in the diclofenac group i.e. 50 mg (11%). The variable doses of both drugs may of course have had an influence on efficacy and safety. The results of the study showed that both lornoxicam and diclofenac significantly reduced overall pain up-to 4 weeks. However till 4 weeks lornoxicam proved to have significantly more potency and efficacy and better adverse effect profile than diclofenac. Adverse reactions, especially gastrointestinal side effects were the commonest in both the groups. NSAID-typical adverse events such as diarrhoea, nausea, retching occurred with both the drugs. Typical GI symptoms, however, occurred less frequently during treatment with lornoxicam. One patient showed hypersensitivity as itching in palms which was mild and subsided in 4 days. These results imply that lornoxicam has benefits in terms of less frequent and less intense adverse events when compared to diclofenac.

Serious reactions were not reported in both the groups; however it should be noted that both the drugs were not used in their maximally tolerated doses. The tolerability of lornoxicam is also superior to that of diclofenac, since more patients reported adverse events during intake of the diclofenac. With its short plasma elimination half-life of 4h, lornoxicam contributes to a good tolerability. While the analgesic effects are still evident, protective prostaglandins may recover. The higher efficacy and less frequent and less intense adverse effects of lornoxicam may be because of differences regarding mechanism of action. In a study it was found that of the panel of NSAIDs tested, lornoxicam was found to be the most potent balanced inhibitor of human COX-1/-2. The equipotent COX-isoenzyme inhibition by lornoxicam is complemented by a marked inhibition of IL-6 production and of Inos-derived NO formation [17]. This may be responsible for better tolerability of lornoxicam. Osteoarthritis is a chronic illness. NSAIDs are valuable for the initial few weeks as they definitely produce analgesic effect. However the analgesic effect is not sustained for longer periods by both the drugs. Discontinuation rates with NSAIDs are high in OA patients and this probably accurately reflects their limited clinical value [18].

CONCLUSION

Lornoxicam and diclofenac both are effective as analgesics in patients suffering from osteoarthritis (OA) for short term. Lornoxicam is more effective than diclofenac. Lornoxicam is better tolerated than diclofenac.

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