

# Study of Efficacy and Tolerance of Ketoprofen and Diclofenac Sodium in the Treatment of Acute Rheumatic and Traumatic Conditions

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I.A. Jokhio, A. Ali ( Departments of Orthopaedics, Dow Medical College, Karachi. )

K.A. Siddiqui, M. Abbas ( Liaquat Medical College Hyderabad. )

T Waraich ( Nishtar Medical College, Multan. )

## Abstract

A comparative, multi-centre study, was conducted during June to December, 1996 to evaluate the efficacy and tolerance of Ketoprofen 100mg Enteric Coated (EC) tablet and 100mg intra-muscular injection; with that of Diclofenac Sodium 50 mg tablet and 75 mg intra-muscular injection in acute rheumatic and traumatic disorders. Total of 180 patients (90 per drug), were studied, 82 men and 98 women, between the ages of 18 and 75 years. The symptoms and the number of patients were backache 50, arthritis 64, frozen shoulder 32 and sprains 34. Pain was qualitatively assessed by visual analogue scale (VAS), XY pain index, pain at mobilization and the level of pain handicap. For pain (VAS 75-100) the treatment was initiated with an injectable bid, followed by tablets bid or tid. If the pain score on VAS was less than 75, tablets were given in a bid dosage. The duration of treatment was 15 days in each case. The overall complete relief of symptoms occurred in 25% (23/90) patients with Ketoprofen and in 10% (9/90) diclofenac sodium. Moderate to mild relief was found in 75% (67/90) cases with Ketoprofen and 87% (78/90) with diclofenac sodium. No pain relief was seen in 3% (3/90) with diclofenac sodium, as against no failure in pain relief in the ketoprofen group. Tolerance was found as excellent-good for ketoprofen in 72% (65/90) with diclofenac sodium in 50%, moderate to poor for ketoprofen in 28% (35/90) and with diclofenac sodium in 50% (45/90). Our results indicate that ketoprofen compared to diclofenac sodium is efficacious in acute rheumatic and traumatic injuries. Ketoprofen injection, compared to diclofenac sodium was found to be more effective in providing analgesia (JPMA 48:373, 1998).

## Introduction

The management of acute soft tissue injuries need rest, anti-inflammatory and analgesic therapy. The inflammatory response that follows soft-tissue trauma is associated with swelling and pain. NSAIDs are effective in reducing swelling and relieving pain in acute rheumatic and traumatic conditions. Although, arthritic conditions are usually chronic and need long-term management, their acute phase needs urgent management. The wide variety of NSAIDs available in the market, presents a dilemma for the clinician while choosing the exact therapeutic measure. Both ketoprofen and diclofenac sodium are well established analgesic and anti-inflammatory agents. Their use in acute rheumatic and traumatic conditions has been studied internationally. However, in the absence of local data, this study became imperative.

## Patients and Methods

A multi-center comparative study was planned to evaluate the efficacy and tolerance of ketoprofen and diclofenac sodium in acute rheumatic and traumatic conditions. The form of drugs used were: ketoprofen 100mg EC tablet and 100mg intra-muscular injection and diclofenac sodium 50mg tablet and 75 mg intra-muscular injection. The dose depended on the severity of patient's condition i.e., if

VAS showed severe pain (VAS 75-100), treatment was initiated by injection bid followed by tablets bid or tid. If the pain score on VAS was less than 75, tablets were given in a bid dosage. Additional treatment like physiotherapy or gel application, if needed, was allowed.

Patients between the ages of 18 and 75, with a history of acute painful rheumatic and traumatic conditions were included, even if they had taken NSAIDs previously. Fractures and injuries with appreciable tearing, cases needing surgery and pregnant ladies were excluded. The study drug was administered on the randomly selected patients for a duration of 15 days.

The efficacy of treatment was judged on the basis of reporting of pain, which was qualitatively evaluated on inclusion day (day 0), day 7 and day 15 of treatment, on the basis of: A) VAS: patient was asked to pinpoint about his condition of pain, on a 20cm scale, labeled as score 0, 25, 50, 75 and 100.

The scale was rated as 0-25 for no-slight pain, >25-50 as mild pain, >50-75 as moderate pain and >75-100 as severe pain. Average score reduction on VAS, was an important criteria for assessment of reduction in pain (i.e., decrease in pain score from 80 to 75, will result in reduction of pain of 15 score), B) XY pain index {X axis was qualified as intense (4), severe (3), medium (2), slight (1) and none (0); whereas the Y axis was based on permanent pain (4), intermittent and waking patient during night and/or occurring on slight activity (3), intermittent and during the normal activity (2), rare (1) and absent (0). Each patient's condition was entered in the relevant box accordingly; C) Pain at mobilization (no pain as 0, pain as 1, pain with grimace as 2, pain with grimace and withdraw! as 3); and D) The level of pain handicap (absence of handicapping pain as 0, moderate pain not preventing normal activity as 1, severe pain seriously limiting normal activity as 2 and severe pain preventing activity as 3). The increase in the number of patients towards the category of '0' will indicate the improvement in the status of pain. Investigator's assessment for efficacy was based on pain relief from above criteria, on the basis of complete relief, moderate to mild relief.

The tolerance was assessed on reporting of side effects, on the basis of excellent (no side effect), good (1 side effect), moderate (2 side effects) and poor (more than 2 side effects).

## **Results**

A total of 180 patients were evaluated; the patient characteristics are given in Table.

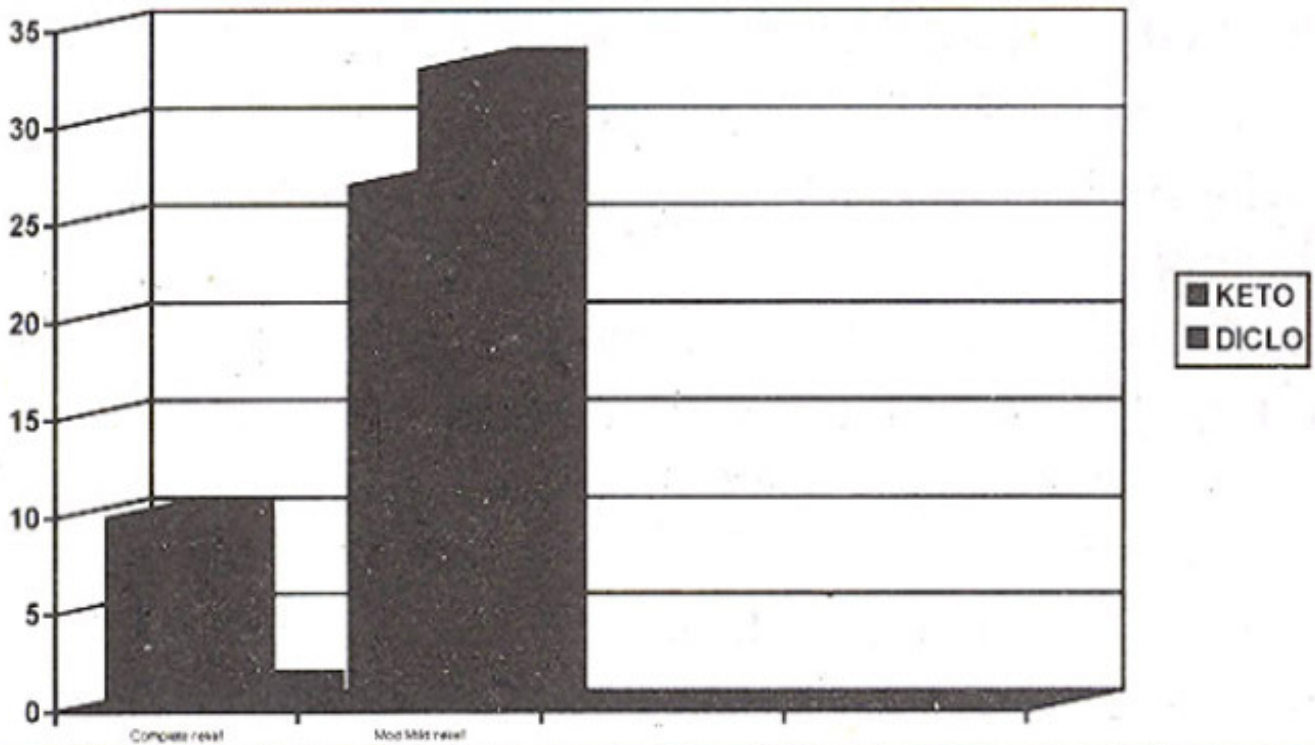
**Table. Patient characteristics (n=180) and indications for treatment at inclusion (day 0).**

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<b>Sex :</b>	
Male	82
Female	98
<b>Age range</b>	18-75
<b>Weight range (kg)</b>	50-75
<b>Indications with No. of patients:</b>	
Low backache and sciatica	50
Arthritis	64
Frozen shoulder	32
Sprains	34

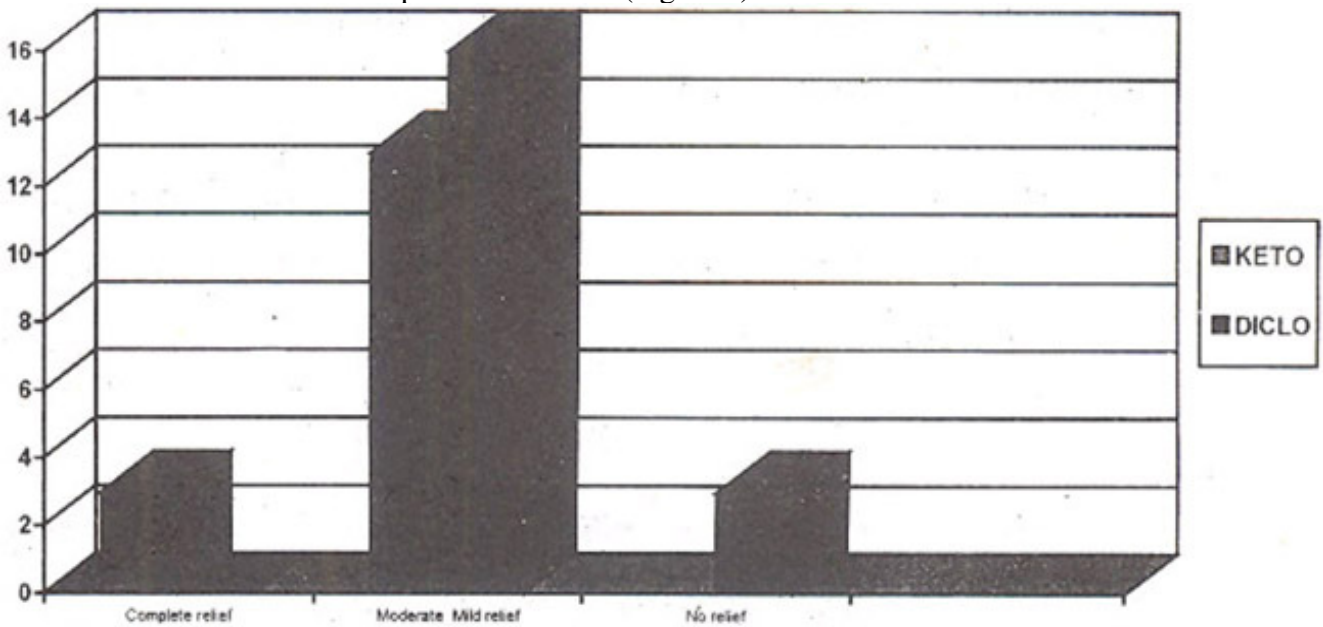
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Following results were achieved, on the basis of pain parameters for the different conditions studied: Arthritis: A total of 64 cases were evaluated, 31 of whom were treated with diclofenac sodium (osteoarthritis knee 25 and rheumatoid arthritis 6) and 33 with ketoprofen (osteoarthritis knee 22, rheumatoid arthritis 10 and gouty knee 1). Ketoprofen injection given in 8% (7/90) cases, resulted in an average reduction of 31 on VAS from day 0 to day 7, whereas diclofenac sodium injection used for 3% (3/90) cases, resulted in average reduction of 23 on VAS from day 0 to day 7. Based on all the pain parameters, complete pain relief occurred with Ketoprofen in 10% (9/90) patients and with diclofenac sodium in 1% (1/90) patients. Moderate to mild relief with ketoprofen was seen in 27% (24/90) and with diclofenac sodium in 33% (30/90) (Figure 1).



**Figure 1. Pain relief with ketoprofen and diclofenac sodium in arthritis.**

Frozen shoulder: Out of 32 patients in this category (15 had ketoprofen and 17 diclofenac) only 1 case for each drug, the injectable form was used and the reduction in score was almost similar. In 2 cases with diclofenac sodium, intraarticular steroid therapy was given. Based on all the pain parameters, complete pain relief was obtained in 3% (3/90) cases with ketoprofen and none with diclofenac. Moderate to mild relief occurred in 13% of cases (12/90) with ketoprofen and in 16% (14/90) with diclofenac sodium. There was no relief of pain in 3% cases (Figure 2).



**Figure 2. Pain relief with ketoprofen and diclofenac sodium in frozen shoulder.**

Sprains: Out of total 34 patients (15 had ketoprofen and 18 diclofenac sodium), 4% (4/90) were

initiated with ketoprofen injection which resulted in an average reduction of 45 on VAS from day 0 to 7, whereas with diclofenac sodium 7% (6/90) cases were started on injectables with an average reduction of 38 on VAS from day 0 to day 7. The overall results show that ketoprofen resulted in complete relief in 7% cases (6/90), whereas cases on diclofenac sodium showed relief in 4% (4/90). Moderate to mild pain relief with ketoprofen was 10% (9/90) and that with diclofenac sodium was 16% (14/90) (Figure 3).

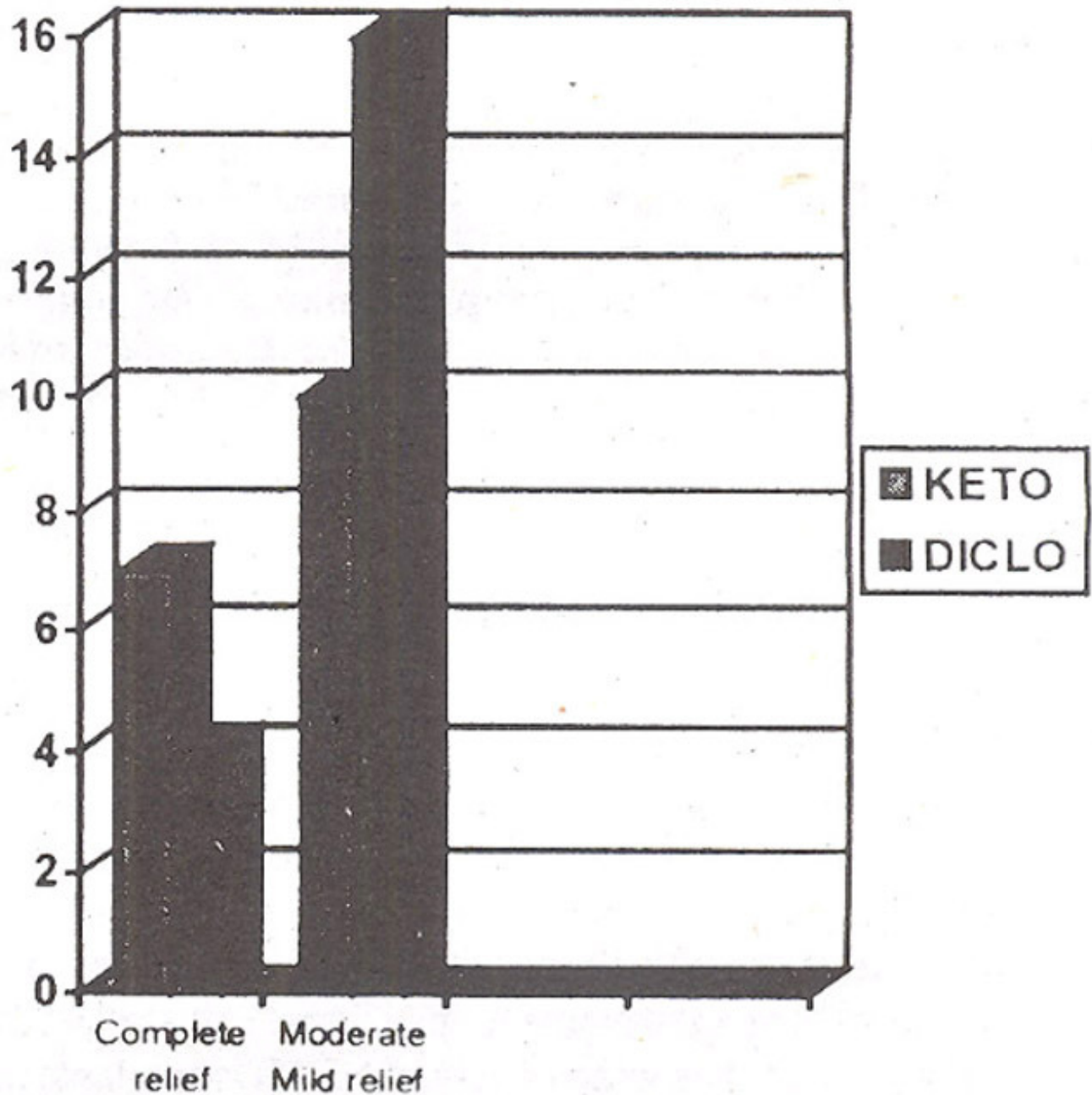


Figure 3. Pain relief with ketoprofen and diclofenac sodium in sprains.

Backache: Out of total of 50 cases (26 for ketoprofen and 24 for diclofenac sodium), injectable theEapy was given to 6% (5/90) patients with ketoprofen and the average reduction of 24 was seen on VAS from day 0 to 7. Diclofenac sodium injection was used in 3% (3/90) cases and average reduction of 23 was present on VAS from day 0 to day 7. In one case the patient had earlier taken diclofenac and other analgesics and then ketopmfen was given, resulting in relief in symptoms. Complete relief was found in

6% (5/90) cases with ketoprofen and 1%(1/90)withdiclofenac sodium. Moderate to mild relief with ketoprofen was 23% (21/90) and with diclofenac sodium 22% (20/90) (Figure 4).

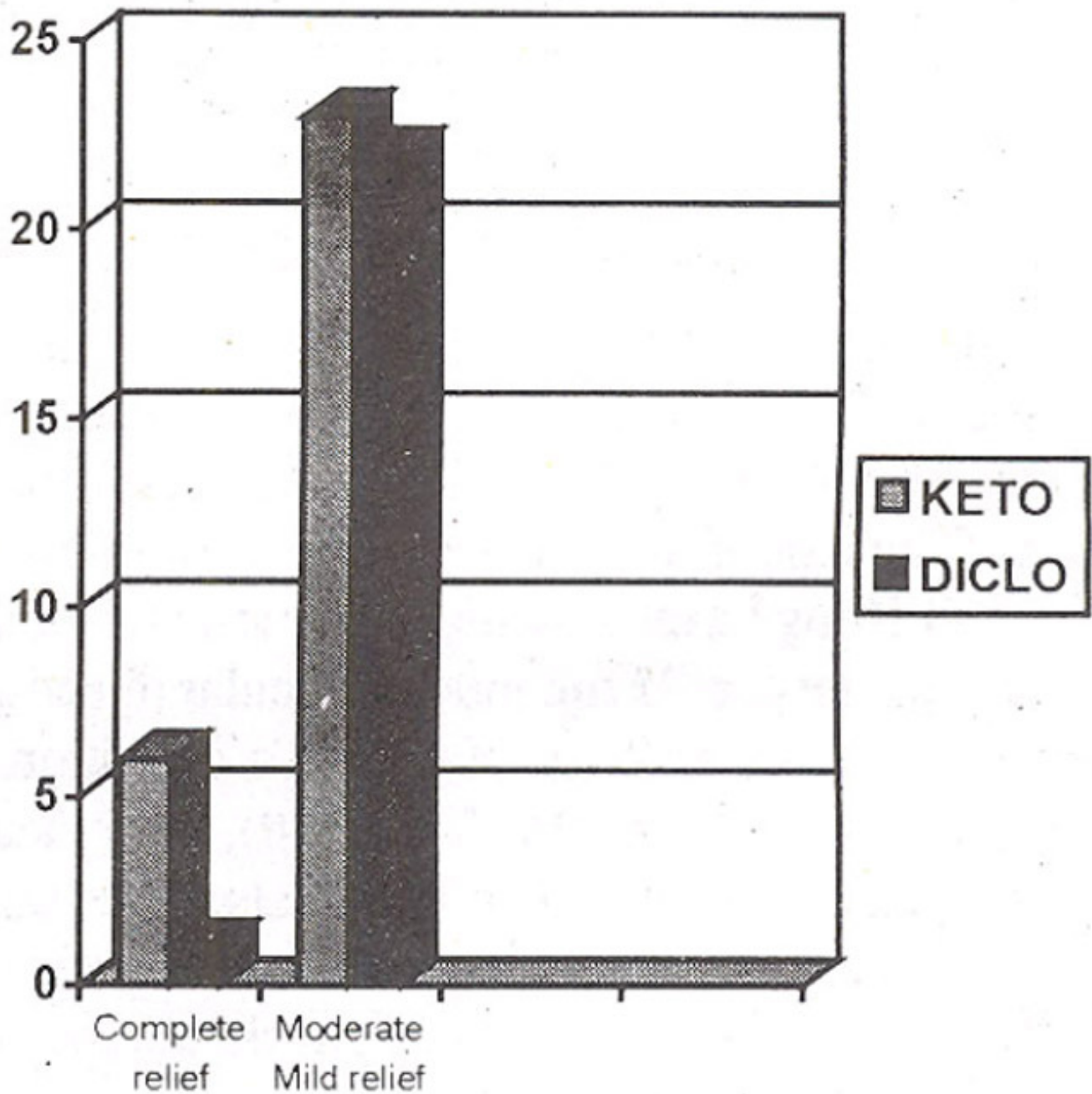


Figure 4. Pain relief with ketoprofen and diclofenac sodium in backache.

Injections of ketoprofen and diclofenac sodium were used in 19% (17/90) and 14% (13/90) respectively. The average reduction in pain score was better with ketoprofen as compared to diclofenac sodium (Figure 5).

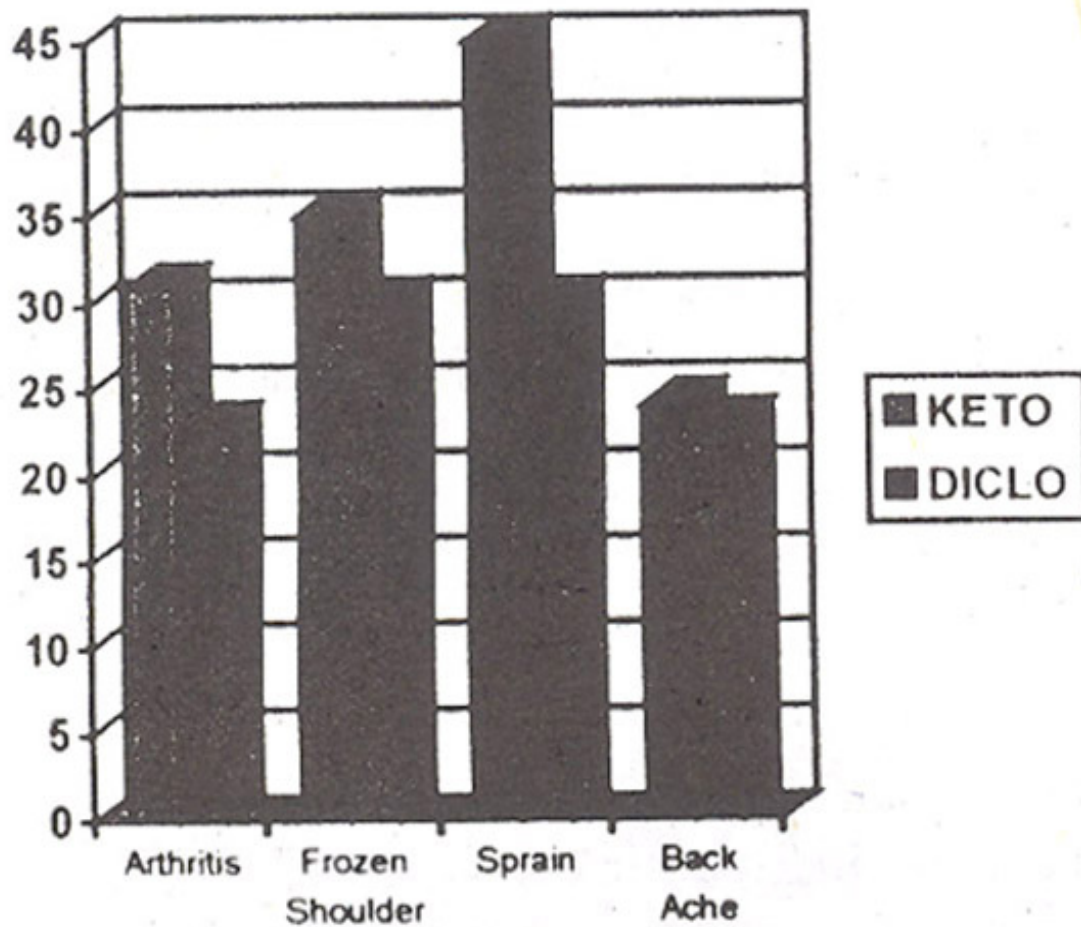
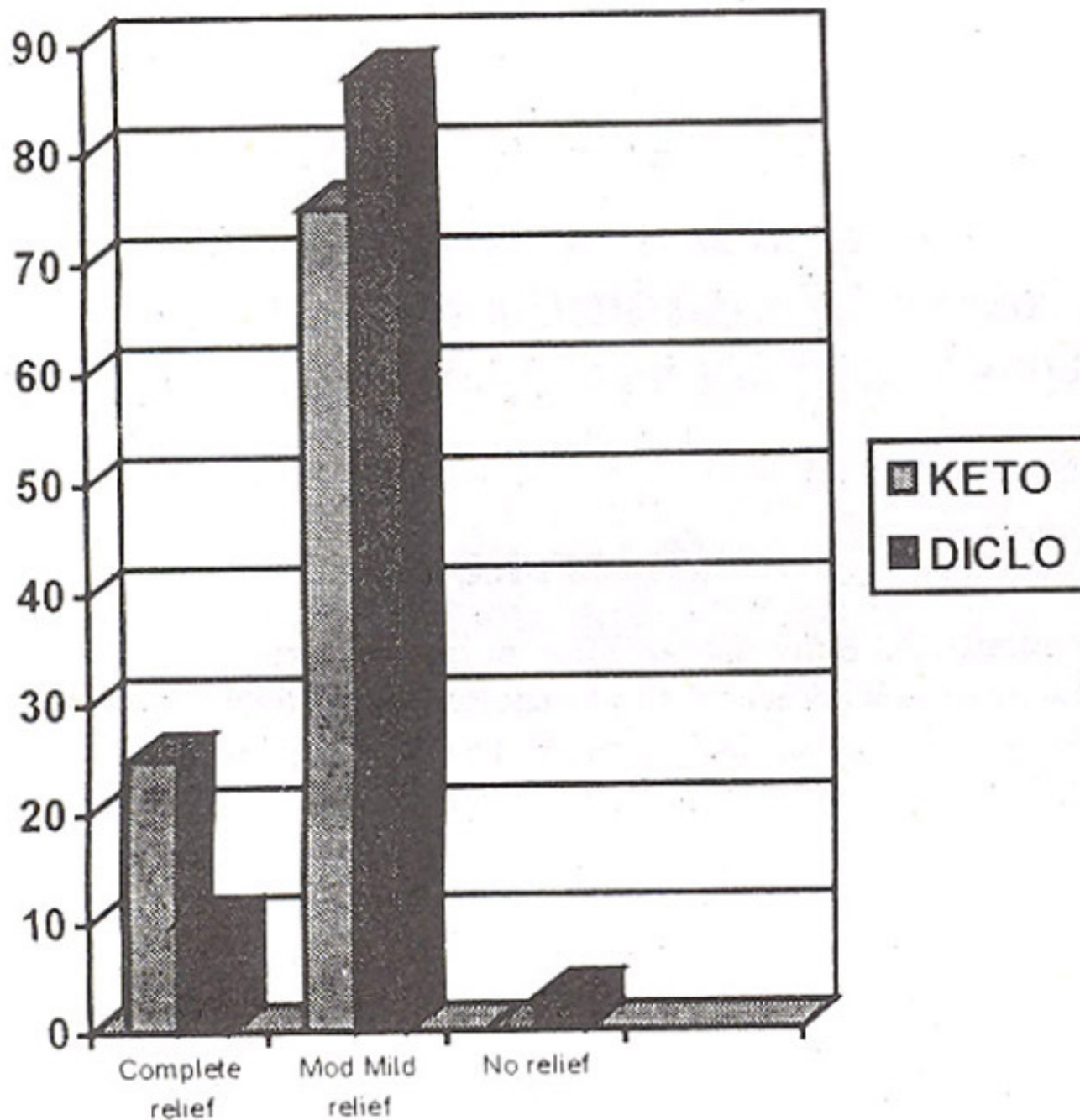


Figure 5. Efficacy for ketoprofen and diclofenac sodium injections on the basis of average pain score.

The overall investigators' assessment of efficacy revealed that complete relief with ketoprofen in 25% (23/90) cases and with diclofenac sodium in 10% (9/90) cases. Moderate to mild relief was found 75% (67/90) cases with ketoprofen and with diclofenac sodium in 87% (78/90). No pain relief was present in 3% (3/90) with diclofenac sodium as against no failure in pain relief in the ketoprofen group (Figure 6).



**Figure 6. Cumulative results of efficacy of ketoprofen and diclofenac sodium.**

The tolerance for ketoprofen was excellent in 31.11% (28/90), good in 44.4%(40/90)and moderate to poor in 24.4% (22/90). With diclofenac sodium excellent in 12.2% (11/90), good in 33.3%(30/90)and moderate to poor in 24.4%(22/90) (Figure 7).



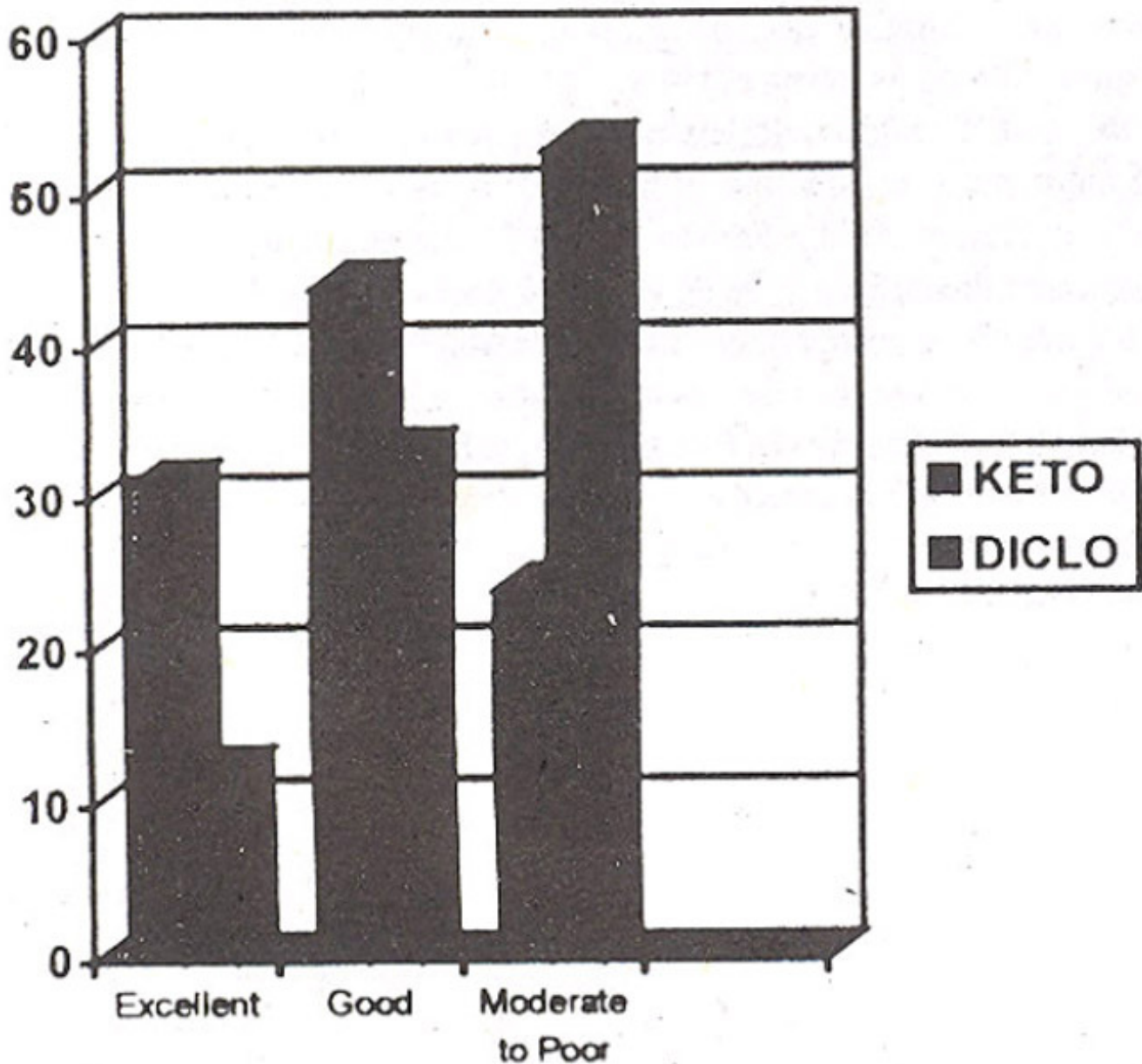


Figure 7. Tolerance between ketoprofen and diclofenac sodium.

### Discussion

The earlier comparative studies conducted with ketoprofen and diclofenac sodium have been performed in different acute conditions. According to Boey<sup>1</sup>, in case of rheumatoid arthritis, both drugs had beneficial effects. In case of coxarthrosis and gonarthrosis similar results were found<sup>2,3</sup>. In another study by Mostini<sup>4</sup> in arthritis, the efficacy was comparable but tolerance was better with ketoprofen than diclofenac. Similar are the findings of our study. According to Di Goorgio et al<sup>5</sup> in a paper on rheumatology, "the difference in favor of Ketopmfen was significant than diclofenac. A study in lumbago by Matsuno et al<sup>6,7</sup>, reveals that effects of ketoprofen were attained earlier than those of diclofenac.

Giordano's<sup>8</sup> study on Ketoprofen injection in painful shoulders syndrome reveals that, this could be recommended as an alternate to local steroid therapy. Another study in the same indication with hemiplegic elderly patients<sup>9</sup> and with combination of lidocaine 2% reveals significant pain reduction both at rest and after either active or passive mobilization.

In case of acute sports injuries, in comparison with ibuprofen<sup>10</sup>, the results have shown that, Ketoprofen had a significantly faster onset of pain relief than ibuprofen after the first dose<sup>11</sup>. In an open multicenter study<sup>11</sup> of young subjects affected by osteo-arthromuscular acute injuries (sprains, tendinitis, lacerations, contusions...), the control of pain has shown their fast gradual improvement as regards both intensity and frequency.

With this background, if we analyze the results of our study, it would reveal that, in low backache and Sciatica, arthritis and sprains, the efficacy results of the two drugs are comparable, however in case of frozen shoulder Ketoprofen has shown better results compared to Diclofenac sodium. Ketoprofen has also shown better results in bringing complete pain relief; whereas in moderate to mild pain relief diclofenac sodium has shown similar results. While the efficacy for tablets could not be assessed separately, that for the injectable formulation is possible due to their short duration of treatment. The results reveal that ketoprofen intra-muscular injection has performed better than that of diclofenac sodium.

Thus ketoprofen possesses some special properties, which makes it comparable to diclofenac sodium. We are aware that, an important part of the inflammatory process observed in soft-tissue trauma can be due to the direct effects of prostaglandins liberated locally as a result of tissue damage or to their potentiation of more classical chemical mediators<sup>6</sup>.

Inhibition of both prostaglandin release and synthesis have been attributed to NSAIDs<sup>7</sup>. Ketoprofen has been shown to be a more potent inhibitor of prostaglandin synthesis and rabbit aorta-contracting substance than was indomethacin, naproxén, ibuprofen, phenylbutazone and acetylsalicylic acid in guinea pig lung tissue in vitro study<sup>8</sup>.

In case of chronic conditions like osteoarthritis, the role of ketoprofen is as effective as the currently available therapies<sup>9</sup>. Several studies have been conducted on defining the analgesic role of NSAIDs, in the management of acute soft tissue injuries. In these studies where concomitant physical therapy was administered, four NSAIDs were identified, which were demonstrated unequivocally to provide additional benefits and ketoprofen was one of them. At least for some NSAIDs effects on nociceptive pathways independent of prostaglandin synthesis may explain their analgesic character<sup>10</sup>. In a recent analysis of dental pain model, NSAIDs such as ketoprofen, that can act both peripherally and centrally, are particularly potent in this pain model<sup>11</sup>. Thus, ketoprofen possesses in addition to its peripheral action, a central analgesic action, which makes it distinct from the other NSAIDs.

## **Conclusion**

Ketoprofen and diclofenac sodium are NSAIDs and have been used as an analgesic, since a long time. Our results from the study indicate that ketoprofen is efficacious and tolerable in acute rheumatic and traumatic injuries, compared to diclofenac sodium. Ketoprofen injection was found to be more effective in providing analgesia in most of the conditions studied. We thus recommend the use of ketoprofen injection in acute painful disorders of musculo-skeletal system.

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