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STUDY OF EFFICACY AND TOLERANCE OF KETOPROFEN IN THE TREATMENT OF ACUTE MUSCULOSKELETAL CONDITIONS

BY

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ABSTRACT

Study of efficacy and tolerance of Ketoprofen was performed during April 1995-April 1996, in 13 men and 17 women, between the ages of 18 to 75 years. The indications studied were Cervical Spondylosis (6), Backache {(including Sciatica) (8)}, Osteoarthrosis knee (7), Shoulder pain {(adhesive capsulitis) (4)} Rheumatoid arthritis, Tennis elbow, Plantar fasciitis, and injury knee (4), and osteoarthrosis of hip (1).

Pain was qualitatively studied through various parameters, like visual analogue scale and others, through Ketoprofen enteric coated 100mg tablets, twice a day, for 10 days. The overall assessment after the treatment showed that, 80% were better, whereas 17% remained unchanged, and 3% became slightly worse. There were no reported side effects. Results from the study indicate that enteric coated Ketoprofen 100mg, is efficacious in the treatment of acute musculoskeletal conditions.

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INTRODUCTION

Modern treatment of acute soft tissue injuries consists of ice compression, rest, and analgesic treatment, rather than previous therapies of heat, rest and massage. In case of rheumatic conditions, the mainstay is rest, anti-inflammatory and analgesic therapy. The inflammatory response that follows soft-tissue trauma is associated with swelling and pain. Considering this component in the acute phase of the injury, and the need of non-steroidal anti-inflammatory drugs (NSAIDs') in rheumatic conditions.

NSAIDs' should be effective in reducing swelling and relieving pain in acute rheumatic and traumatic conditions. Ketoprofen is a recognized analgesic and anti-inflammatory agent used in the treatment of rheumatic and traumatic injuries. Due to its properties, its efficacy and tolerance was studied in a ten day treatment of acute musculoskeletal conditions.

MATERIAL AND METHODS

To be included in the study, men and women between the ages of 18 and 75, had to give informed consent and history of acute painful rheumatic and traumatic conditions. Fractures and injuries without appreciable tearing, and cases needing surgery, were excluded.

Each patient was given Ketoprofen enteric coated 100mg tablets, twice a day for 10 days. Additional treatment, if needed, was allowed, and patients who had taken NSAIDs' previously, were also included in the study.

Pain was qualitatively evaluated on inclusion and day 10 of treatment, on the basis of: **A. Visual Analogue Scale (VAS):** Patient was asked to pinpoint on the scale about his condition of pain. 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; **B. XY pain index:** X axis was qualified as intense (4), severe (3). medium (2), slight (1), and none (0). whereas, 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 according to his/her condition; **C. Pain at mobilization:** In this parameter, no pain was classified as 0, pain as 1, pain with grimace as 2. pain with grimace and withdrawal as 3; and **D. The level of pain handicap:**

The assessment was on the basis of 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 improvement in the status of pain.

The efficacy of the treatment was judged by the above mentioned pain parameters, and further interviewing patient after the treatment on how they feel, with statements like, much better, better, slightly better, unchanged, slightly worse, and worse.

Tolerance was assessed on the basis of reporting of side effects, on the basis of excellent, good moderate, and poor.

RESULTS

Thirty patients, 13 men and 17 women, between the ages of 18 and 75, completed the trial. The indications studied were Cervical Spondylosis; Backache (including Sciatica), Osteoarthrosis knee and hip; Shoulder pain, Rheumatoid arthritis, Tennis elbow, Plantar fasciitis, and injury knee (table-1).

TABLE - 1

PATIENT'S CHARACTERISTICS AND INDICATIONS ON INCLUSION (day 0); n = 30

Sex	
Male	13
Female	17
Age (in years)	18 - 75
Weight (in kg.)	50 - 75
History of NSAID	
Yes	17
No	13
Indications with # of patients:	
Neck pain (Cervical Spondylosis)	6
Backache (including Sciatica)	8
Osteoarthrosis knee	7
Shoulder pain	4
Osteoarthrosis hip Rheumatoid arthritis Tennis elbow Plantar fasciitis Injury knee	5

The pain parameters used, and their results show the following status of pain parameters:

VAS (table - 2): The minimum range 0-25 had no patient on day 0, and 16 on day 10; whereas, the maximum range of severe pain >75-100, had 5 patients on day 0, and only "1" on day 10.

TABLE - 2

VISUAL ANALOGUE SCALE

Parameters	On day 0		On day 10	
	n	%	n	%
no-slight pain: (0-25)	0	0	16	53.33
mild pain: (>25-50)	19	63.33	9	30
moderate pain: (>50-75)	7	23.33	4	13.33
severe pain: (>75-100)	4	13.33	1	03.33

XY pain index (table - 3): The 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).

The relevant boxes were filled on the basis of status of pain. The product of X and Y scale, was taken as the parameter for analysis. For eg. if the intensity of pain was (4) on day 0 and the nature was permanent pain (4), then the product would be 16. Similarly, if the intensity of pain was slight (1), and the nature as rare pain (1), then the product would be 1. Same was applied for the other parameters of X and Y.

Thus, the decrease in the resultant of the product of X and Y, would indicate the improved status of the patient.

The results show the product range of 16-9, for "10" patients on day 0, and for "5" on day 10. The product range of 8-4 for "20" patients on day 0, and "14" on day 10. Whereas the product range of 3-0 had "0" patients on day 0 and "11" on day 10.

TABLE - 3

XY PAIN INDEX

Parameters	On day 0		On day 10	
	n	%	n	%
Intensity x nature:				
4x4-3x3	10	33.33	5	16.66
4x2-2x2	20	66.66	14	46.66
3,2,1,x1 and 0	0	0	11	36.66

Status of patients on Day 0					
Intensity:	4	3	2	1	0
x					
Nature:					
4	2	0	0	0	0
3	4	4	2	0	0
2	8	4	5	0	0
1	1	0	0	0	0
0	0	0	0	0	0

Status of patients on Day 10					
Intensity:	4	3	2	1	0
x					
Nature:					
4	1	0	0	3	0
3	1	3	0	0	0
2	0	3	2	0	0
1	6	4	6	1	0
0	0	0	0	0	0

Pain at mobilization (table - 4): This was categorized by: No pain as 0, pain as 1, pain with grimace as 2, pain with grimace and withdrawal as 3.

In category 0, there were none patients on day 0, and "3" on day 10. In category 1, there were "14" patients on 0, and "19" on day 10, in category 2, there were "13" patients on day 0 and "8" patients on day 10, whereas in category 3, there were "3" patients on day 0 and "0" on day 10.

TABLE - 4

PAIN AT MOBILIZATION

Parameters	On day 0		On day 10	
	n	%	n	%
no pain (0)	0	0	3	10
pain (1)	14	46.66	19	63.33
1+grimace (2)	13	43.33	8	26.66
2+withdrawl (3)	3	10	0	0

The pain handicap (table - 5): It was specified on the basis of: 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 results show that, in category 0, there were no patients on day 0; whereas there were "11" on day 10. In category 1, "16" patients were recorded on day 0; only "10" remained on this state on day 10. In category 2, "14" patients were present on day 0, and only "9" remained on day 10. For category 3, there were "3" patients on day 0, with none on day 10.

TABLE - 5

PAIN HANDICAP ON DAY 0 AND 10

Parameters	On day 0		On day 10	
	n	%	n	%
Absence of handicapping pain (0)	0	0	11	36.66
Moderate pain not preventing normal activity (1)	16	53.33	10	33.33
Severe pain seriously limiting normal activity (2)	14	46.66	9	30
Severe pain preventing normal activity (3)	0	0	0	0

The assessment of the patient after the treatment through interviewing showed the status of much better state by "4" patients, better by "11" patients, slight better by "9" patients, unchanged by "5" patients, slightly worse by "1" patient and worse by "none" of the patient. The drug was well tolerated by the patients, and there no reported side effects.

DISCUSSION

The results of this study indicate that after treatment with 100mg of enteric coated Ketoprofen, 80% patients felt better, and there were no reported side effects. This is validated by the findings through the assessment of pain parameters.

The improvement is seen in VAS, through the shift of 53.33% patients in the category of no-slight pain from mild-moderate-severe pain status; and another 33.33% patients in the category of mild pain. Thus a total number of 86.66% patients appearing in the categories of no-mild pain. **Pain index**, the product of intensity and nature of pain on XY scale showed 73.33% patients showing improvement on day 10. **Pain at mobilization**, showed 73.33% patients in the categories of no pain to presence of pain; whereas severe form of pain in the form of pain with grimace, and pain with grimace and withdrawal was present in the others. **Pain handicap** showed 70% patients appearing in the categories of absence of pain and maderate pain not preventing normal activity.

Other trials conducted with indomethacin, administered at a dose of 50mg TID to 15 soccer players suffering from a variety of sprains, strains, and direct injuries, was not superior to placebo in relieving pain, swelling, and duration of disability[1]. In another study, 30 patients with acute ankle sprains were treated for seven days with either phenylbutazone or placebo. There was no acceleration in the reduction in volume of the sprained ankles nor were there any clinical differences in status or pain relief[2]. A ten-day Swedish study of 100 patients with sprained ankles compared 800mg of ibuprofen TID with placebo. No differences were found between the two treatments in the reduction of swelling, pain, or tenderness[3].

In a double-blind study of 65 acute soft-tissue sports injuries treated concurrently with intensive physical therapy and early active rehabilitation, 150mg/day of indomethacin demonstrated a slight but not statistically significant superiority over placebo capsules after a week's therapy[4]. Administration of 150mg/day of indomethacin and placebo in the treatment of 83 patients with traumatic soft tissue lesions, showed statistically significant improvements in the relief of spontaneous pain and swelling and in increased freedom of movement; all of

these differences were observed during the first five days of treatment[5].

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[6]. Inhibition of both prostaglandin release and synthesis have been attributed to NSAIDs'[7]. Ketoprofen has been shown to be a more potent inhibitor of prostaglandin synthesis and rabbit aorta-contracting substance than was indomethacin, naproxen, ibuprofen, phenylbutazone, and acetylsalicylic acid in guinea pig lung tissue in vitro[8]. It is also superior to indomethacin on in vivo and in vitro synthesis of different prostaglandins in response to carragenin-induced edema in the hind paw of rats[9].

In case of chronic injuries like osteoarthritis, the role of Ketoprofen is as effective as the currently available therapies (10).

Several studies have been conducted on defining the analgesic role of NSAIDs', in the management of acute soft tissue injuries. In these studies, 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. Ketoprofen is one of these, which exerts its effect, both through central and peripheral mechanisms (11).

In our study protocol, the dosage given to the patients was two tablets daily. Thus, further improvement in patients condition could have been possible by giving Ketoprofen thrice a day in severe acute conditions.

CONCLUSION

The results of the study showed improvement for all the pain parameters used. The overall assessment at the end of the treatment showed 80% patients in the category of being better, and the drug being well tolerated. Thus, Ketoprofen could be recommended for acute painful disorders of musculoskeletal system.

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