

OPEN LABELED CLINICAL EVALUATION OF LOCAL APPLICATION OF NIMESULIDE TRANSDERMAL GEL IN PAINFUL MUSCULOSKELETAL CONDITIONS

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ABSTRACT

In an open labeled study nimesulide transdermal gel (Nimulid transgel) was evaluated for its efficacy and safety in painful musculoskeletal conditions. The study was conducted at 2 centres viz MAMC & LNJP and AIIMS, New Delhi, over a period of 4 months enrolling 119 evaluable patients. A statistically significant difference was observed in the pain intensity and pain relief during the treatment period in all musculoskeletal conditions except tennis elbow. There was a decrease in tenderness and analgesic intake in all conditions. Also, there was an improvement in the daily activities. There were no side effects observed during the entire study period. The results suggest that Nimulid transgel is efficacious in the treatment of painful musculoskeletal conditions.

Key Words: Musculoskeletal Conditions - Transdermal Gel - Efficacy -Safety

INTRODUCTION

Musculoskeletal complaints account for more than 10 percent of all outpatient evaluations in general medical practice. Many of the musculoskeletal complaints that cause patients to seek medical attention are related to self-limited conditions requiring symptomatic therapy which mainly involves analgesics-particularly non-steroidal antiinflammatory drugs (Cush & Lipsky 1994).

Nimesulide is a non steroidal anti-inflammatory drug which has a sulfonanilide moiety (Swingle etal 1976). In several clinical studies, nimesulide has shown favourable anti-inflammatory, analgesic and antipyretic activity in a variety of inflammatory conditions and pain states such as osteoarthritis, cancer, thrombophlebitis, oral surgery, dysmenorrhoea in adults, general surgery, respiratory tract infections, otorhinolaryngological diseases and traumatic injury (Biscarini 1988, Ward 1988, Davis, 1994). Nimesulide has been proved to be useful in musculoskeletal conditions such as ankle sprain, minor sports injuries and osteoarthritis in studies conducted by various investigators (Dreiser 1993, Calligaris 1993). Also, nimesulide has lesser propensity to cause adverse gastrointestinal effects (Davis 1994 Ward 1988). Furthermore, topically applied transdermal formulation of nimesulide further avoids the typical gastro intestinal symptoms caused by NSAIDs.

The aim of the present study is to evaluate the efficacy and safety of Nimesulide transdermal gel (Nimulid transgel) in patients with painful musculoskeletal conditions.

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MATERIAL AND METHODS

The open labeled trial was conducted in out patients attending the orthopedic clinics at MAMC & LNJP and AIIMS at New Delhi over a period of four months from February to May 1996. The nimesulide transdermalgel (Nimulid transgel) was provided by Panacea Biotec Ltd. for the entire study.

A total of 119 patients of either sex (Male-66, Female-53), between 18-67 years of age with various painful musculoskeletal conditions (Tenosynovitis, bursitis, sports injury, tennis elbow and fibromyalgia) not requiring oral NSAIDs were enrolled in the study after giving their written informed consent. The average weight of the patients was 58 ± 15 kg. The patient demographics are represented in Table 1. Patients with skin lesions and open wounds were excluded from the study.

No. of patients enrolled	119
Age (range)	18 - 67 years
Weight	58 ± 15 kg
Sex (F/M)	53/66

The patients enrolled were advised local application of 1 cm of Nimesulide transdermalgel (Nimulid transgel) per site 3 times a day for a maximum period of seven days. Paracetamol (500 mg.) was the escape medication prescribed, if pain was not controlled with the test drug.

The patients were evaluated on day 0, day 2, and day 7 for the following parameters: Pain intensity - on a 100 mm visual analogue scale; pain relief - on a 100 mm visual analogue scale, tenderness on a 4 point scale (0-absent, 1-tender, 2-tender and winced, 3-tender, winced and withdrew);

escape analgesic use (paracetamol tablets); daily activities on a 4 point scale (0 - no discomfort, 1 - mild discomfort, 2 - moderate discomfort and 3 - marked discomfort) and side effects such as rash, pruritus, itching, redness or erythema.

RESULTS:

A total of 119 patients were enrolled in the study. The diagnostic break up and the mean duration of the presenting symptoms are given in Table 2 and Table 3 respectively. The past history of NSAID intake for the presenting symptoms was positive in 53 /119 i.e. 44.53% of the patients enrolled.

Condition	Number of patients
Tenosynovitis	21
Bursitis	13
Sports injury	19
Tennis elbow	23
Fibromyalgia	43
Total	119

Condition	Duration	Mean no. of sites
Tenosynovitis	4 Weeks	2
Bursitis	4 Weeks	2
Sports injury	3 Days	1
Tennis elbow	6 Weeks	1
Fibromyalgia	4 Weeks	1

Table 4 shows the effect of Nimesulide transdermal gel (Nimulid transgel) in tenosynovitis. The pain intensity decreased from 76 mm (day 0) to 7 mm (day 7) on visual analogue scale and the pain relief was 55% by day 2 itself. Tenderness was also found to disappear by day 7. The escape analgesic intake decreased from a mean of 3 to 0.45. The performance of daily activities improved from a mean score of 2 to 0 (i.e. normal).

Condition	Parameter	Day 0	Day 2	Day 7
Tenosynovitis (N=21)	Pain intensity (0-100 mm)	76	45	7
	Pain relief (0-100 mm)	0	55	93
	Tenderness	2	1	0
	Analgesic intake	3	1.3	0.45
	Daily activities	2	1	0
	Side effects	nil	nil	nil

The efficacy of nimesulide in bursitis is presented in Table 5, The pain intensity decreased to 9 mm on day 7 with a pain relief of 57% by day 2 and 91% by day 7- A decrease in the tenderness and

analgesic intake was observed along with an improvement in the daily activities.

Table 5: Effect of Nimesulide transdermal gel (Nimulid transgel) on clinical parameters in bursitis

Condition	Parameter	Day 0	Day 2	Day 7
Bursitis (N=13)	Pain intensity (0-100 mm)	79	43	9
	Pain relief (0-100 mm)	0	57	91
	Tenderness	2	1	0
	Analgesic intake	3.6	1.8	0.56
	Daily activities	2	1	0
	Side effects	nil	nil	nil

Table 6 shows the improvement in the parameters studied in cases of sports injury on the application of nimesulide transdermal gel. The pain relief was 97% by day 7 and the tenderness decreased from a mean score of 3 to 0 by day 7. The analgesic intake decreased and there was a definite improvement in the daily activities.

Table 6: Effect of Nimesulide transdermal gel (Nimulid transgel) on clinical parameters in sport injuries

Condition	Parameter	Day 0	Day 2	Day 7
Sport injuries (N=19)	Pain intensity (0-100 mm)	87	42	3
	Pain relief (0-100mm)	0	58	97
	Tenderness	3	1	0
	Analgesic intake	2	1	0.42
	Daily activities	2	1	0
	Side effects	nil	nil	nil

Table 7 represents the efficacy of nimesulide transdermal gel in fibromyalgia. Pain intensity decreased from 86 mm to 6 mm by day 7 on the visual analogue scale with a pain relief of 94%. There was decrease in tenderness and analgesic intake. The daily activities improved from a mean score of 3 to 0.

Table 7: Effect of Nimesulide transdermal gel (Nimulid transgel) on clinical parameters in fibromyalgia

Condition	Parameter	Day 0	Day 2	Day 7
Fibromyalgia (N=23)	Pain intensity (0-100 mm)	86	41	6
	Pain relief (0-100 mm)	0	59	94
	Tenderness	3	1	0
	Analgesic intake	3	1.7	1
	Daily activities	3	2	0
	Side effects	nil	nil	nil

The efficacy of nimesulide transdermal gel is depicted in Table 8. The pain intensity decreased from 81 mm (day 0) to 46 mm on day 2 and to 12 mm on day 7 with a pain relief of 88% at the end of therapy. There was only slight improvement in tenderness and daily activities scores with little decrease in the analgesic intake.

Table 8: Effect of Nimesulide transdermal gel (Nimulid transgel) on clinical parameters in fibromyalgia

Condition	Parameter	Day 0	Day 2	Day 7
	Pain intensity (0-100 mm)	81	46	12
	Pain relief (0-100 mm)	0	54	88

Pain relief (0-100 mm)	0	54	88
Tenderness	3	2	1
Analgesic intake/day	3	2.2	1.4
Daily activities	2	1	1
Side effects	nil	nil	nil

Table 9 shows the efficacy of nimesulide transdermal gel in all the groups together. The mean intensity of pain in all groups was 43.4 mm on day 2 and the intensity of pain was only 7.4 mm on day 7. The mean pain relief was 56.4 mm on day 2 and 92.6 mm on day 7. Tenderness decreased from a mean score of 2.6 to 0.48 by day 7. There was a significant decreases in the analgesic intake and an improvement in the daily activities.

Condition	Parameter	Day 0	Day 2	Day 7
All groups (N=119)	Pain intensity (0-100 mm)	81.8	43.4*	7.4*
	Pain relief (0-100 mm)	0	56.4*	92.6*
	Tenderness	2.6	1.24*	0.48*
	Analgesic intake	2.92	1.6*	0.76*
	Daily activities	2.2	1.2*	0.2*
	Side effects	nil	nil	nil

* p ≤ 0.05 by Chi² test.

DISCUSSION

Musculoskeletal conditions are a common problem following injuries or strenuous exercise for which many non steroidal anti - inflammatory drugs are available over the counter. Oral formulations have gastrointestinal side effects therefore topical application of the drug would be good to avoid these gastrointestinal adverse effects.

Nimesulide transdermal gel (Nimulid transgel) is a novel transdermal drug delivery system with enhanced drug absorption characteristics. From the results it can be seen that there is significant improvement in all the parameters studied on application of the nimesulide transdermal ge (Nimulid transgel) formulation in all the groups. There was statistically significant reduction in the pain intensity and pain relief parameters as shown by Chi² test (p < 0.05) in all groups combined together. There was statistically significant improvement in the other parameters such as tenderness, analgesic intake and daily activities both on day 2 and day 7 as shown by Chi² test (p < 0.55).

Nimesulide transdermal gel is effective in all musculoskeletal conditions with the order of efficacy being sports injury > fibromyalgia > tenosynovitis > bursitis > tennis elbow, as shown by the pain relief on day 7. In case of Tennis elbow, nimesulide transdermal gel was not as effective as in the other conditions. Nimesulide transdermal gel was perhaps less effective in tennis elbow patients who had the condition for a mean period of 6 weeks as opposed to 4 weeks in tenosynovitis. bursitis and fibromyalgia and 3 days in sports injuries.

Throughout the study no side effects were observed and the nimesulide transdermal gel was found to be well tolerated. Therefore nimesulide transdermal gel can be advocated for long term use in cases of musculoskeletal problems.

The results of this study indicate that Nimesulide transdermal gel is effective in patients with painful musculoskeletal conditions of different etiologies. A significant reduction in oral analgesic intake was observed. Nimesulide transdermal gel (Nimulid transgel) can thus be advantageously used in musculoskeletal problems alone or as an additive with oral NSAIDs.

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