

Efficacy and Tolerability of Nimesulide in Post Operative Pain of Anorectal and Inguinoscrotal Surgery

RL Gupta*, A Chaudhary**, H C Sethi***, S Sharma****,
M Mahajan*****, Corresponding Author Sangeeta Sharma*****

Abstract

In the present open labeled multicentric trial, 176 patients scheduled for anorectal and inguinoscrotal surgery were included. Nimesulide 100 mg (Brand used : Nimulid) relieved pain approximately half an hour after administration and intensity of pain reduced significantly from 4th hour onwards and was maintained with Nimesulide 100 mg twice daily dose for four days. The analgesia provided was sufficient, only 33 (18.75%) patients needed rescue therapy with pethidine on the 1st day and it decreased to 11 (6.25%) patients at the end of 5 days. Therapy with Nimesulide was well tolerated and analysis of liver and kidney function tests and haemogram revealed no clinically significant changes at the end of therapy.

Introduction

Post operative pain is a major problem after surgery. It appears to be related to inflammation and is most often treated with nonsteroidal anti-inflammatory drugs (NSAIDs). Nimesulide is a nonsteroidal anti-inflammatory drug that possesses anti-inflammatory, analgesic and antipyretic properties which have been demonstrated in animal models and confirmed in clinical studies². In common with other NSAIDs, Nimesulide inhibits cyclo-oxygenase but also acts as a scavenger of oxygen free radicals². Furthermore Nimesulide has the added benefit of being well tolerated by the gastric mucosa³ as compared with other NSAIDs viz diclofenac, piroxicam and ketoprofen. Nimesulide has been successfully used in several therapeutic fields including oral¹, general⁶ and gynaecological⁴ surgery but experience with this regimen appears to be somewhat limited in India. The present study was conducted to assess the efficacy and tolerability of Nimesulide when administered orally to patients after anorectal or inguinoscrotal surgery.

Patients and Methods

All patients of either sex between the age of 20 -70 years scheduled for anorectal and inguinoscrotal surgery were recruited in the study after obtaining informed consent. Patients with serious renal, hepatic, cardiac, endocrine, metabolic, pulmonary or neurological disorders, hypersensitivity to NSAIDs and alcoholics were excluded. Pregnant and lactating women were also excluded from the study. Patients received oral Nimesulide 100 mg twice daily except on first day. The first dose of Nimesulide was administered orally 2 hours after surgery alongwith some milk. The second dose was administered at 8 pm on the day of the operation. From the second day until fourth day Nimesulide 100 mg was administered at 8 am and 8 pm. Surgery was performed under spinal or local anaesthesia.

No other NSAIDs were allowed during the study. Sedatives were administered on demand one hour after the night dose of Nimesulide. All patients received prophylactic treatment with laxatives and antibiotics. Efficacy of the treatment was assessed by evaluating pain intensity. Pain intensity was measured on a 100 mm visual analogue scale every half an hour for 2 hours and every 2 hours for 12 hours after the first dose of Nimesulide. Subsequently intensity and relief of pain were evaluated at intervals of 6 hours.

Table 1 : Patient characteristics

Total number of Patients	176
Male	139
Female	37
Age distribution (years)	Number of cases (%)
20-21	21 (11.36)
21-30	67 (37.9)
31-40	46 (26.3)
41-50	32 (18.8)

51-60	6 (3.4)
61-70	5 (3.4)
Diagnosis	
Haemorrhoids	36 (20.45)
Fistula-in-ano	32 (18.18)
Fissure-in-ano	20 (11.36)
Hydrocoele	54 (30.68)
Hernia	20 (11.36)
Varicocoele	14 (7.95)
<i>No significant difference between age and sex distribution</i>	

Table 2 : Effect of first dose of Nimesulide 100 mg as measured by visual analogue scale (VAS) during first twelve hours

Time after surgery (n)	VAS (mean ±SD)
at base line	100±100
0.5	46.65±34.15
1	48.09±30.34
1.5	45.21 ±27.45
2	33.21 ±98.87
4	*31.0±19.10
6	*27.42±19.80
8	*30.42±20.70
10	*31.58±22.10
12	*33.21 ±23.60

*P<0.05

Tolerability was assessed by performing routine blood (haemogram, liver function test and kidney function test) before and after completion of therapy. Spontaneous reporting was used to assess tolerability.

The doctor assessed efficacy using a scale (0 same as current drug; 1 worse than current drug; 2 slightly better than current drug; 3 moderately better than current drug; 4 markedly better than current drug). Investigators considered the following parameters for rating: onset of analgesic effect, duration of action, need for sedatives, hypnotics and adverse effect profile.

Differences in pain intensity and other variables were analysed by students t-test or chi square to assess statistical significance as appropriate. P<0.05 was considered as statistically significant.

Table 3 : Effect of Nimesulide 100mg 12 hourly on pain intensity on Visual Analogue Scale (VAS)

Day after surgery	Time of the day	VAS Score (mean±SD)	T value
Day 1	6 AM	29.79±18.50	4.00*
	10 PM	17.95±16.14	7.12*
Day 2	6 AM	21.63±15.72	5.88**
	10 PM	12.16±12.24	8.66**
Day 3	6 AM	15.19±13.06	7.44**
	10PM	8.49±10.82	9.87**
Day 4	6 AM	11.35±14.02	8.30**
	10 PM	4.58±11.57	10.84**

*P<0.05 **P<0.01

Results

A total of 176 patients (139 male, 37 female) scheduled for anorectal and inguinoscrotal surgery were enrolled (Table 1). The demographic variables were analysed to ascertain homogeneity in age, sex distribution and type of surgery involved. The differences were not statistically significant, Table 2

shows that analgesic action began approximately half an hour after administration and intensity of pain reduced significantly from 4th hour onwards and was maintained thereafter till 12 h ($p < 0.05$). The intensity of pain reduced from 100 mm to 31 mm on VAS at the end of 4 hours and by the end of protocol therapy the intensity of pain was only 4.5 mm (Table 3). Further more, the analgesia provided was adequate. Only 33 (18.75%) patients needed rescue therapy with pethidine on the 1st day and it decreased to 11 (6.25%) at the end of 5 days.

Nimesulide was rated as markedly better than existing therapy by the investigators in 103 (58.52%), moderately better in 62 (35.22%), slightly better in 4 (2.27%), same as current drug in 2 (1.1 %) and worse than the current drug in 5 (2.84%) patients (Table 4).

Analysis of liver and kidney function tests and haemogram revealed no clinically significant changes at the end of therapy (Table 5).

Discussion

The results of the present study show that Nimesulide has analgesic activity similar to other NSAIDs when administered orally in post operative pain. These results corroborate the findings of studies demonstrating the efficacy of Nimesulide in the treatment of patients for anorectal surgery⁷, general surgery⁵ and when administered rectally in patients undergoing hernioplasty or mastectomy^{5,6}.

Table : 4 Investigators' Global Assessment of efficacy of Nimesulide in relieving pain associated with various types of surgical procedures.

Diagnosis	Worse (%)	Same (%)	Slightly better (%)	Moderately better (%)	Marketedly better (%)	Total
Haemorrhoids	1 (2.77)	2 (5.55)	0	7 (19.44)	26 (12.22)	36
Fistula-in-ano	0	0	0	25 (78.12)	7 (21.88)	32
Fissure-in-ano	0	0	0	6 (30)	14 (70)	20
Hydrocoele	2 (3.7)	0	2 (3.7)	15 (28.57)	35 (64)	54
Hernia	2 (10)	0	2 (10)	4 (20)	12 (60)	20
Varicocoele	0	0	0	5 (37)	9 (63)	14
Total (%)	5 (2.84)	2 (1.13)	4 (2.27)	62 (35.22)	103 (58.52)	176 (100)

Table : 5 Effect of Nimesulide on Laboratory Parameters

Test	Initial	Final
Haemoglobin (gm%)	12.8	12.7
Total WBC (Per cumm)	7056	7234
Differential Count	P61, L34, E3, M2	P66, L30, E2, M2
SGOT (IU/L)	27.98	28.05
SGPT (IU/L)	24.79	24.73
S.Alk. Phosphatase (IU)	8.50	8.72
Blood Urea Nitrogen (mg%)	25.10	25.05
Serum creatinine (mg%)	1.36	1.42

In conclusion, Nimesulide 100 mg BD is an alternative to the therapy with diclofenac and other NSAIDs usually administered by intravenous or intramuscular route for the treatment of post operative surgical pain and inflammation.

Acknowledgment

We express our gratitude to Panacea Biotec Ltd. for supporting and providing us Nimulid Tablets (Nimesulide) for the entire study.

References

1. Bucci E, Mignogna D, Scaricabarozzi I, Bucci L, Lo Muzio L, et al. Studio Clinico sull'attività terapeutica e la tollerabilità della nimesulide in formulazione supposte in odon tostomatologia. *Minerva Stomatologica PO* 1990; 10:827-831.
2. Davis R, Brogden RN. Nimesulide: an update of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy. *Drugs* 1994; 48:431-454.
3. Marini U, Spotti D. Gastric tolerability of Nimesulide: A double blind comparison of 2 oral dosage regimens and placebo. *Drugs* 1993; 46 (suppl 1), 249-252.
4. Montoneri C, Garofalo A, Iurato S, Scaricabarozzi I, Trezzani R, Studio clinico full efficacia e La tollerabilità della nimesulide in formulazione supposte in confronto al Hurbiprofen in ginecologia. *Minerva Ginecologica* 1990; 42: 413-419.
5. Romella G, Costagli V, Vetere M, Capra C, Casella G, Sogin A, Scaricabarozzi I. Comparison of nimesulide and diclofenac in the prevention and treatment of pain and inflammatory postoperative complications of general surgery. *Drugs* 1993; 46 suppl 1: 159-161.
6. Stafanoni G, Saccomanno F, Scaricabarozzi I, Volontieri G, Persiani I, et al. Efficacia clinica della nimesulide in confronto a diclofenac sodico nella prevenzione e nel trattamento della sintomatologia algicoflogistica post chirurgica. *Minerva Chirurgica* 1990; 23: 1469-1475.
7. Zuccurman, M, Panconesi R, Scaricabarozzi I, Nara ML, Bechi P. Clinical efficacy and tolerability of nimesulide compared with naproxen in the treatment of post haemorrhoidectomy pain and inflammation. *Drugs* 1993; 46 suppl 1, 177-179.

* *Professor* Department of Surgery University College of Medical Sciences & GTB Hospital, Delhi

** *Professor* Department of Gastrointestinal Surgery GB Pant Hospital New Delhi

*** *Consultant* Department of Surgery SMS Medical College Jaipur

**** *Asstt. Professor* Dept. of Psychopharmacology IHBAS, Delhi

***** *Research Officer* Dept. of Surgery University College of Medical Sciences & GTB Hospital, Delhi

***** *Asst. Professor* Dept. of Psychopharmacology IHBAS, Delhi