

# Comparative Clinical Study of Free Radical Scavenging Antiinflammatory Agent Nimesulide with Other Conventional NSAIDS in Different Operative Procedures

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## Summary

The present study was conducted on 200 obstetrical and 160 gynaecological patients admitted in UISEM, Kanpur from Dec. 1997 to Nov 1998. The obstetric patients faced episiotomy and LSCS during their delivery. The patients were kept in identical antenatal, intranatal and postnatal care and medication but were different in type of acute inflammatory drug administered. The different drugs selected for study were conventional nonsteroidal drugs such as Ibuprofen and Diclofenac, protease preparation serratiopeptidase and free radical scavenging agents as nimesulide. On this basis obst. and gynae. patients were divided in 4 sub groups of 25 patients and 40 patients each respectively. These subgroups were compared with each other on the basis of prior decided criteria for wound healing. For sake of comparison a scoring system was devised. The cases with better healing had more score. The drug subgroups were compared to each other by average wound healing score as well as by the individual criteria found with the drugs. The comparison groups were also tested for significant relation. Thus the clinical efficacy and tolerability of the various anti-inflammatory drugs was clinically compared. In the clinical trial Nimesulide was found better in the clinical efficacy to conventional nonsteroidal drugs. Ibuprofen was having maximum side effects. Serratiopeptidase needed supplementation of anti-inflammatory effect and had delayed onset of action.

## Introduction

There has always been a clinical dilemma regarding the ideal anti-inflammatory agent whenever a surgical wound is made, so that there is minimal post-operative pain and tenderness at the site and faster wound healing and of course with fewer side effects. Our clinical study endeavours to find out the superiority of 2<sup>nd</sup> generation NSAIDS over conventional agents, if any. Anti-inflammatory drugs act by inhibition of cyclooxygenase. It exists in two forms – COX<sub>1</sub> and COX<sub>2</sub>. Conventional NSAIDS as ibuprofen and diclofenac reversibly inhibit both COX<sub>1</sub> and COX<sub>2</sub>. COX<sub>2</sub> inhibition accounts for anti-inflammatory analgesic antipyretic role of NSAIDS but COX<sub>1</sub> inhibition causes side effect as gastrointestinal ulceration and intolerance, blockade of platelet aggregation and hypersensitivity reactions. Newer anti-inflammatory agents as nimesulide is selective COX<sub>2</sub> inhibitor. It does not inhibit COX<sub>1</sub> therefore the levels of cytoprotective prostaglandins are not reduced and side effects are prevented.

Proteolytic preparations as serratiopeptidase are also claimed to have anti-inflammatory effects owing to lysis of inflammatory exudates, better penetration of antibiotics and absorption of breakdown products in blood.

## Material & Methods

The present study was conducted on 100 patients of lower segment caesarean section and 100 patients with episiotomy and 160 patients of total abdominal hysterectomy admitted in UISE maternity hospital attached to GSVM Medical College, Kanpur from Dec. 97 to Nov. 98.

Their detailed history was recorded through general and systemic examination along with complete obstetrical/gynaecological examination was done. They were investigated completely; and the operation was done. In pre-operative, per-operative and post operative cases management was similar in all patients.

The 100 patients each of lower segment caesarean section and episiotomy studied were divided into four subgroups of 25 cases each namely I, II, III, IV. Similarly patients of total abdominal hysterectomy were subdivided in 4 subgroups of 40 patients each. Each group was different only in the choice of anti-inflammatory agent used. Anti-inflammatory agents used were –

I Ibuprofen	400 mg 8 hrly
II Diclofenac	40 mg 12 hrly
III Serratiopeptidase	10 mg 8 hrly
IV Nimesulide	100 mg 12 hrly

A separate wound healing score was made for convenience of comparison between the different subgroups. Following criteria were followed to build up a wound healing score (WHS) (Table I).

### Observation & Discussion

In lower segment caesarean section group we observed that nimesulide required minimum days for effective anti-inflammatory action i.e. 8.32. These were maximum with serratiopeptidase viz. 15.28, while the diclofenac they were 8.56 and with ibuprofen 10.56 (Table I).

Minimum time required for episiotomy wound healing was 6.68 days in nimesulide group, while 7.48 8.00 and 8.12 days with ibuprofen serratiopeptidase and diclofenac respectively. Side effects were minimum in nimesulide group (16%) while maximum in ibuprofen group (48%) i.e. tolerability was maximum with nimesulide. This is in contrast to study done by Calligaris et al (1993) in traumatic sport lesions.

As shown in Table I anti-inflammatory drugs were needed for 8.4, 9.0, 11.6, and 14.8 days with nimesulide, ibuprofen, diclofenac and serratiopeptidase respectively in caesarean section group. Similar results were obtained by Rossi et al (1991) in ENT inflammatory pathologies.

Side effects in lower segment caesarean section were least with nimesulide, 92% cases being free of any side effects. Side effects were maximum viz 40% with ibuprofen causing mainly gastrointestinal intolerance. Similar results were obtained by Stefanoni et al (1990) and Ramella et al (1993).

Rate of complications was minimum in nimesulide subgroup (8%) and maximum in serratiopeptidase group (64%). Anti-inflammatory effect was complete at its own in nimesulide group, while it needed to be supplemented in all other groups, maximally with serratiopeptidase in 64% cases (Table II).

None of the episiotomy wounds got complicated by nimesulide, while maximally complicated wounds were seen with serratiopeptidase (64%). Diclofenac too revealed lower complication rate (16%) than ibuprofen (36%) potentiation of anti-inflammatory effect was minimally needed by nimesulide (12%) and ibuprofen (20%) while it was maximally demanded by serratiopeptidase (80%). All episiotomy wounds followed were healthy in nimesulide group. But with ibuprofen, serratiopeptidase and diclofenac only 60%, 68% and 76% wounds were found to be healthy (Table II). This proves clinical efficacy of nimesulide. Minimum side effects with nimesulide were observed by Facchini et al (1993) while studying fractures in children.

In TAH group side effects were minimum (20%) with nimesulide and 40% and 50% and 60% with diclofenac, serratiopeptidase and ibuprofen respectively. These results are comparable to those of Cunetti et al (1993) in pyrexia of elderly (Table II).

No complication of postoperative wound is seen in 80% cases in nimesulide and ibuprofen group. Anti-inflammatory effect was complete in 80% cases with diclofenac, 70% cases with nimesulide, 60% cases with ibuprofen and 50% cases with serratiopeptidase (Table II). Similar clinical efficacy between nimesulide and ibuprofen was obtained by Zuckermann et al (1993) in relief of pain and oedema of post-surgical wounds.

In lower caesarean section group wound scar was healthy and linear in all cases treated with nimesulide, while only in 78%, 80% and 60% cases with ibuprofen, diclofenac and serratiopeptidase respectively.

In caesarean section, maximum wound healing score of 14.6 in maximum number of cases (25) was attained by nimesulide score while it was minimum (10.76) with diclofenac (Table II).

Maximum episiotomy healing score was attained by nimesulide (13.96) and minimum 11.8 with ibuprofen. Results within all comparison groups showed statistically significant differences ( $p < 0.01$ ). Thus, in our study drug of choice for episiotomy wound is nimesulide, followed by serratiopeptidase, diclofenac and ibuprofen respectively. This is in contrast to study done by Agus et al (1993) on anti-inflammatory treatment of superficial thrombophlebitis.

In total abdominal hysterectomy group abdominal stitch line as well as vaginal vault was healthy in 80% cases in nimesulide while 70%, 40% and 20% cases in diclofenac, ibuprofen and serratiopeptidase groups respectively.

**Table I**  
**Significance of Different Criteria healing**

Criteria	Episiotomy group				LSCS group				TAH group			
	I	II	III	IV	I	II	III	IV	I	II	III	IV
1. Days required for healing	7.48	8.12	8.0	6.68	10.56	8.56	15.28	8.32	9.0	11.6	14.8	8.4
2. Side effects												
Nil	52%	68%	60%	84%	60%	78%	80%	92%	40%	60%	50%	80%
Minor	48%	32%	40%	16%	40%	12%	20%	8%	60%	40%	50%	20%
Major	-	-	-	-	-	-	-	-	-	-	-	-
3. Complication												
None	64%	74%	36%	100%	76%	68%	36%	92%	80%	60%	50%	80%
Immediate	36%	16%	32%	-	24%	32%	64%	8%	20%	40%	50%	20%
Late	-	-	-	-	-	-	-	-	-	-	-	-
4. Other drug required												
No drug	80%	64%	20%	88%	60%	68%	36%	100%	60%	80%	50%	70%
One drug for <6 days	40%	16%	48%	12%	40%	12%	44%	-	40%	-	50%	30%
One drug for >6 days	-	20%	32%	-	-	20%	20%	-	-	20%	-	-
5. Stitch line												
Healthy Linear	60%	76%	68%	100%	78%	80%	60%	100%	40%	70%	20%	80%
Healthy Uneven	40%	24%	32%	-	10%	5%	20%	-	60%	30%	20%	20%
Ragged	-	-	-	-	12%	15%	20%	-	-	-	60%	-

**Table - II**  
**Comparison between Different Sub-Groups LSCS-Group**

Comparison Groups	Mean score	Standard Deviation	't'	'p'
I-D				
I	$X_1 = 13.36$	$S_1 = 2.09$	3.88	< 0.01
II	$X_2 = 10.76$	$S_2 = 2.55$		
I-S				
I	$X_1 = 13.36$	$S_1 = 2.09$	0.66	> 0.05
II	$X_2 = 12.88$	$S_2 = 2.94$		
I-N				
I	$X_1 = 13.36$	$S_1 = 2.09$	2.58	< 0.05
IV	$X_2 = 14.60$	$S_2 = 2.55$		
D-S				
II	$X_1 = 10.76$	$S_1 = 2.55$	2.68	< 0.01
III	$X_2 = 12.88$	$S_2 = 2.94$		
D-N				
II	$X_1 = 10.76$	$S_1 = 2.55$	6.86	< 0.01
IV	$X_2 = 14.60$	$S_2 = 1.10$		
S-N				
III	$X_1 = 12.28$	$S_1 = 2.94$	2.73	< 0.01
IV	$X_2 = 14.60$	$S_2 = 1.10$		

**Episiotomy Group**

Comparison Groups	Mean score	Standard Deviation	't'	'p'
I-D				
I	$X_1 = 11.08$	$S_1 = 0.87$	5.80	< 0.01
II	$X_2 = 12.76$	$S_2 = 1.15$		
I-S				
I	$X_1 = 11.08$	$S_1 = 0.87$	0.66	>0.05
II	$X_2 = 11.76$	$S_2 = 1.15$		
I-N				
I	$X_1 = 11.08$	$S_1 = 0.87$	12.76	<0.01
IV	$X_2 = 13.96$	$S_2 = 0.70$		
D-S				
II	$X_1 = 12.76$	$S_1 = 1.15$	3.30	<0.01
III	$X_2 = 11.76$	$S_2 = 0.95$		
D-N				
II	$X_1 = 12.76$	$S_1 = 1.15$	4.40	<0.01
IV	$X_2 = 13.96$	$S_2 = 0.70$		
S-N				
III	$X_1 = 11.76$	$S_1 = 0.95$	5.00	<0.01
IV	$X_2 = 13.96$	$S_2 = 0.70$		

**TAH - Group**

Comparison Groups	Mean score	Standard Deviation	't'	'p'
I-D				
I	$X_1 = 13.0$	$S_1 = 0.88$	0.15	< 0.05
II	$X_2 = 12.9$	$S_2 = 1.88$		
I-S				
I	$X_1 = 13.0$	$S_1 = 0.88$	3.08	>0.05
II	$X_2 = 10.5$	$S_2 = 1.34$		
I-N				
I	$X_1 = 13.0$	$S_1 = 0.88$	0.49	<0.05
IV	$X_2 = 14.1$	$S_2 = 1.15$		
D-S				
II	$X_1 = 12.9$	$S_1 = 18.8$	3.12	<0.05
III	$X_2 = 10.5$	$S_2 = 1.34$		
D-N				
II	$X_1 = 12.9$	$S_1 = 1.15$	4.40	<0.05
IV	$X_2 = 14.1$	$S_2 = 0.70$		
S-N				
III	$X_1 = 10.5$	$S_1 = 1.34$	4.20	<0.01
IV	$X_2 = 14.1$	$S_2 = 1.15$		

I-D - Comparison groups of Ibuprofen Vs. Diclofenac  
 I-S - Comparison groups of Ibuprofen Vs. Serratiopeptidase  
 I-N - Comparison groups of Ibuprofen Vs. Nimesulide  
 D-S - Comparison groups of Diclofenac Vs. Serratiopeptidase  
 D-N - Comparison groups of Diclofenac Vs. Nimesulide  
 S-N - Comparison groups of Serratiopeptidase Vs. Nimesulide

In caesarean section group all comparison groups were significantly related except for Ibuprofen Vs Serratiopeptidase ( $t=0.66$  and  $p > 0.05$ ). Thus, in our study nimesulide was drug of choice for post-caesarean wound followed by serratiopeptidase, diclofenac and ibuprofen in that order. Similar results were obtained in ENT. post operative wound trials done by Nouri et al (1993) and Ferrari et al (1993).

't' value (table II) of TAH comparison group ibuprofen Vs serratiopeptidase, diclofenac Vs serratiopeptidase, serratiopeptidase Vs nimesulide was 3.08%, 3.12 & 4.20 respectively i.e. 'p' is significant in all ( $< 0.05$ ). Thus, in our study serratiopeptidase was better than ibuprofen and diclofenac and nimesulide was better than serratiopeptidase.

### Conclusion

The drug of choice for caesarean section, episiotomy and total abdominal hysterectomy is nimesulide, serratiopeptidase, diclofenac and ibuprofen in that order. Nimesulide was better in clinical efficacy, tolerability and rapidity of action than other anti-inflammatory drugs. Serratiopeptidase was the second line of choice but taking longer duration to act, associated with more number of complications and requiring other additional anti-inflammatory drugs. Ibuprofen was found to be associated with more number of side effects mainly

gastrointestinal. Diclofenac though inferior to nimesulide in efficacy and duration of action was associated with lesser side effects.

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