DOUBLE BLIND RANDOMIZED COMPARATIVE EVALUATION OF NIMESULIDE AND PARACETAMOL AS ANTIPYRETICS

Praveen Kumar Goyal, Jagdish Chandra, Unnikrishnan G, Sudarshan Kumari and Susan M. Passah

From the Department of Pediatrics, Kalavati Saran Children's Hospital and Lady Hardinge Medical College, New Delhi 110 001.

Reprint requests: Prof. Jagdish Chandia, Flat No 1, Lecturer's Flats, Lady Hardinge Medical College Campus, New Delhi 110 001.

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Objective: *To compute the efficacy and safety of nimesulide and paracetamol as antipyretic agents* ***Design:*** *Double blind, landonnzed clinical trial* ***Methods:*** *Hospitalized patients having fever due to a variety of infections were given either ding in a randomized manner (Nimesulide group = 49, Paracetamol group = 50) Serial axillary temperature was recorded after drug administration and side effects monitored Results The mean temperature after one hour of drug administration was significantly lower in nimesulide group ($p < 0.05$) Significantly fever doses of nimesulide were required to bung down the temperature on the first day ($p < 0.001$) The mean maximum temperature recorded on second and third day was significantly lower in the nimesulide group ($p < 0.05$) Adverse reactions were seen in the form of epigastric pain and vomiting m one patient in Nimesulide group and three in paracetamol group* ***Conclusion.*** *Nimesulide is more effective than paracetamol as an antipyretic agent and is safe for use in infants and children*

Key words: *Antipyretic, Nimesulide, Paracetamol.*

NIMESULIDE is a relatively new nonsteroidal anti-inflammatory drug (NSAID) Some studies have shown its better antipyretic effect than paracetamol, mafenamic acid and salicylates(l-3) The suspension form of the drug has recently become available in India Hence, this study was undertaken to compare the antipyretic effect and safety of nimesulide with that of paracetamol using the □abeledsion form

Subjects and Methods

Hospitalized children having temperature > 38 5°C were enrolled in this randomized, double-blind prospective study after obtaining an informed consent from patient's parents/guardian Severely ill patients suffering from circulatory collapse, blood dyscrasias, cardiac or hepatic disease, G-6-PD deficiency or meningitis were excluded from the study as were those with history of hypersensitivity to NSAIDs Children having collagen vascular diseases or malignancy as a primary or underlying cause of fever and those receiving antimicrobials and/or corhcosteroids within 24 hours preceding the study were also excluded Nimesulide (Nimulid suspension-Panacea Biotec) and paracetamol were coded as NSAID-A or NSAID-B in a blind manner Children were randomly assigned to receive NSAID-A or NSAID-B. Both preparations were in liquid form and

identical in color. The concentration of the drug was so adjusted that a similar volume of the syrup provided either nimesulide 1.5 mg/kg or paracetamol 10 mg/kg.

Axillary temperature was recorded before drug administration and every half an hour for the first 3 hours of each dose on first day and thereafter every 4 hours on subsequent days or till fever susbided. If temperature remained above 39°C for one hour, tepid sponging was done. In absence of response to tepid sponging, ibuprofen (10 mg/kg) was administered as a rescue drug. Heart rate and blood pressure were monitored before and after each dose of medication throughout the treatment period. Maximum temperature and number of doses of the study drugs required to normalize temperature were recorded. Observation was continued for upto 72 hours after the enrolment in the study. Patients were withdrawn early from the study if body temperature increased above 40°C or decreased below 35 °C, if any severe physical event occurred or if the consent was withdrawn by the parents/guardians.

Renal and liver functions tests, blood sugar level, hemogram and urine analysis were obtained before starting therapy and at the end of study. All adverse events were recorded. Data was analyzed using paired and unpaired Students 't' tests and Chi square test. At the end of the study, drug labels were decoded and drug labelled NSAID-A was found to be nimesulide and NSAID-B was found to be paracetamol.

Results

One hundred and three patients were enrolled in the study; 51 patients (29 male and 22 female) received nimesulide and 52 (34 male and 18 female) received paracetamol. Two patients were excluded from nimesulide group due to loss to follow up while 2 patients were excluded from paracetamol group, one each due to gastrointestinal hemorrhage and lack of response. Thus, 99 patients were evaluable, with 49 of them having received nimesulide and 50 having received paracetamol. The two groups were comparable ($p > 0.05$) for age, sex ratio, baseline body temperature and diagnoses *(Table 1)*. All but one received appropriate antimicrobial therapy for the underlying infections. As shown in *Table II,* the body temperature at enrolment was comparable in both the study groups. The mean body temperature 30 minutes after the first dose and at one hour were significantly lower in the nimesulide group ($p < 0.05$). More patients in paracetamol group (76%) were febrile one hour after drug administration as compared to nimesulide group (61%; $p < 0.05$). At 2 hours, a significantly lower number of patients in the nimesulide group required rescue drug- than in the paracetamol group (6% *vs* 26%; $p < 0.01$). As shown in *Table U,* the mean body temperature in the nimesulide group remained significantly lower than paracetamol group between day 1 to day 3. On day 1, a significantly lower number of nimesulide doses were required to lower body temperature to normal (1.48 *vs* 2.04 doses of paracetamol; $p < 0.001$). However, on day 2, this difference was not significant (1.03 doses of nimesulide vs. 1.02 of paracetamol doses; $p > 0.05$). More doses of paracetamol were required as the mean duration between 2 doses was 8.21 hours compared to 9.8 hours in nimesulide treated patients ($p < 0.05$).

Adverse reactions were seen in the form of epigastric pain and vomiting in one patient in nimesulide group and three patients in paracetamol group. Two patients showed rise in SGOT and SGPT level after paracetamol therapy while none of the patients in nimesulide group had such a rise.

TABLE I-*Patient Characteristics at the Beginning of the Study*

Characteristics	Nimesulide (n = 49)	Paracetamol (n = 50)
1 Age (mo)		
(i) Mean	33.41 ± 31. 37	39 .72 ± 33.72
(ii) Range	1.75 – 60	3.0 – 54.0
2 Male Female (%)	59. 41	68 .32
3 Diagnosis – No. (%)		
Acute respiratory infections	29 (59)	32 (64)
Enteric fever	7 (14.29)	5 (10)
Post measles bronchopneumoma	2 (4.08)	4 (8)
Tuberculosis	3 (6.12)	-
Septicemia	7 (14.29)	4 (8)
Others	1 (2.0)	5 (10)

TABLE II- *Comparison of Mean Temperature in the Nimesulide and Paracetamol Treated Patients on Different Study Days*

Mean body temperature	Nimesulide (n = 49)	Paracetamol (n = 50)
Baseline	38. 5 ± 0.07	38 .6 ± 0. 05
30 min	37. 8 ± 0.08	38 .2 ± 0. 10
1 h	37. 2 ± 0.06	37 .5 ± 0. 03
Second day	37. 4 ± 0.80	38 .0 ± 0.06
Third day	36 9 ± 0.05	37 4 ± 0 .08

Except the baseline temperature, all differences between the groups were statistically significant

Discussion

This study indicates that in children nimesulide has a faster and longer lasting antipyretic effect as compared to paracetamol Similar results have been obtained in another study(l) Nimesulide has also been reported to be atleast as efficacious as or better than naproxen, aspirin, ketoprofen and mefenamic acid in pediatric patients with various medical and surgical conditions(2-8)

The therapeutic effects of NSAIDs are largely the result of their ability to inhibit prostaglandin synthesis via inhibition of cyclo-oxygenase Nimesulide is a relatively weak inhibitor of prostaglandin synthesis *m vitro* and appears to exert its effects through a variety of mechanisms including free radical scavenging, effects on histamine release and activity, neutrophil myeloperoxidase, platelet aggregation and synthesis of platelet activating factor(4)

In nimesulide group, no significant side effect other than mild gastrointestinal symptoms were observed Many earlier studies m children have also shown absence of significant side effects with this drug(2,6) The reported side-effects include

excessive perspiration, heart burn, flushing and skin rash following nimesulide use The frequency of these side-effects tends to increase with a longer duration of therapy(4,9)

In conclusion Nimesulide is a safe drug for use in children which has an antipyretic effect greater than paracetamol.

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