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RESEARCH ARTICLE

A COMPARATIVE STUDY EVALUATING THE SAFETY AND EFFICACY OF PARACETAMOL AND MEFENAMIC ACID IN FEBRILE CHILDREN

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Abstract

Background: Fever is one of the most common symptoms in paediatric practice. Paracetamol and mefenamic acid are frequently prescribed antipyretics, but comparative data on their safety and efficacy in children are limited.

Objective: To compare the safety and efficacy of paracetamol and mefenamic acid in the management of fever in children.

Materials and Methods: A prospective, randomized, comparative clinical study was conducted in the paediatric inpatient at paediatricdep artment of MGM Medical College and Hospital,Aurangabad.Atotalof 1 20 children aged 1 year to 14 years with documented fever{temp>99.5º Farenheit} were enrolled and randomly assigned to receive either oral paracetamol (10-15 mg/kg) or oral mefenamic acid (4-8 mg/kg) at recommended dosing intervals. Temperature reduction was assessed at baseline and at regular intervals1 hour, 4 hours and 6 hours then repeat the cycle for recording bodytemperaturepost-administration. Adverse drug reactions were monitored throughout the treatment period. Data were analysed using appropriate statistical tests, with $p < 0.05$ considered significant.

Results: Both paracetamol and mefenamic acid significantly reduced body temperature from baseline at all measured time points ($p < 0.05$). The mean time to achieve normothermia was slightly shorter in the mefenamic acid group, though not statistically significant. Adverse effects were mild and self-limiting, with gastrointestinal discomfort being the most common in the mefenamic acid group.

Conclusion: Both paracetamol and mefenamic acid are effective and well-tolerated antipyretics in children. Mefenamic acid may offer a marginally faster onset of fever reduction, but paracetamol remains preferable in children with a risk of gastrointestinal intolerance.

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Introduction: -

Fever is a common reason for pediatric OPD visits, causing discomfort and parental anxiety, necessitating prompt management [1,2]. It is a physiological response mediated by pyrogenic cytokines, which increase the hypothalamic set point via prostaglandin E2 (PGE2), leading to elevated body temperature [3-5]. High-grade fever can cause dehydration, febrile seizures, and metabolic complications, warranting antipyretic therapy [6]. Paracetamol is widely used as an antipyretic and analgesic in children, while NSAIDs such as mefenamic acid and ibuprofen provide antipyretic effects by inhibiting cyclooxygenase (COX) and reducing PGE2 synthesis [7-9]. Aspirin, previously used, is now avoided in children due to the risk of Reye's syndrome [10,11]. Paracetamol is well absorbed, metabolized in the liver, and excreted renally; however, overdose can lead to hepatotoxicity requiring N acetylcysteine treatment [12-15]. Mefenamic acid, a non-selective COX inhibitor, has antipyretic and analgesic activity but may cause gastrointestinal and hematological adverse effects [16-19]. Nimesulide, although effective, is avoided in children due to hepatotoxicity [20-22]. The choice of antipyretic should consider efficacy, safety, adverse effect profile, and cost [23,24]. Paracetamol is recommended at 10–15 mg/kg/dose every 4–6 hours (maximum 60 mg/kg/day) and is included in the WHO Essential Medicines List for children [25-27]. NSAIDs may offer effective temperature control but are associated with higher gastrointestinal and renal adverse effects [28-30]. Increased use of mefenamic acid is noted in cases where paracetamol fails to control fever [31].

Comparative studies on paracetamol and mefenamic acid in pediatric fever have shown variable outcomes. Loya et al. found that high-dose paracetamol (20 mg/kg) and mefenamic acid (6 mg/kg) were more effective than standard-dose paracetamol (15 mg/kg) in reducing fever rapidly [32]. Kunkulol et al. and Khubchandani et al. reported superior temperature reduction with mefenamic acid over paracetamol [33,34]. Other studies, including those by Joshi et al. and Kauffman et al., found ibuprofen marginally more effective than paracetamol [35,36], while Vyas et al. observed that a paracetamol-ibuprofen combination reduced fever more quickly [37]. Lal et al. and Goyal et al. reported similar efficacy between nimesulide and paracetamol, but safety concerns limit nimesulide use [38,39].
Despite multiple antipyretics available, paracetamol remains the first-line choice in children due to its safety and cost-effectiveness, while mefenamic acid is often used when additional analgesic effects are desired. Limited comparative studies highlight the need for further research on the efficacy and tolerability of paracetamol versus mefenamic acid in pediatric febrile illnesses to guide rational antipyretic use.

Materials and Methods: -

The details of the study are as: -

- Study Design: One-year, prospective, open-label, single center, double arm, observational study on febrile children at MGM medical college and hospital Aurangabad Maharashtra, India.
- Study Site: Department of Pharmacology in MGM medical college in collaboration with inpatient department of pediatric general ward, MGM medical college, Aurangabad.
- Study Duration: The study was commenced after the date of approval from Ethics Committee for a period of one year.
- Study Population: The population for this study includes all children from age groups 1 year to 14 years presenting with high fever {temp>99.5ºFarenheit} to IPD meeting the inclusion and exclusion criteria.
- Study Sample Size: For the present study, the sample size was calculated according to the data cited in Kunkulol Rahul et al. (2013).

Eligibility Criteria: -

Inclusion Criteria: -

- All admitted febrile children in pediatric general ward either on Paracetamol or mefenamic acid.
- Patient/attenders ready to give informed consent.
- Patient in the age group of 1 year- 14 years.

Exclusion Criteria: -

- Uncooperative patients.
- Patients not following the protocol.
- Severely ill patients requiring ICU admission.

Methodology: -

The present observational study was carried out in the Inpatient Department (IPD) of the Paediatric General Ward at MGM Medical College and Hospital, Aurangabad, among febrile children. Patients were enrolled based on predefined inclusion and exclusion criteria. Written informed consent was obtained from the parents or legally authorized representatives (LARs) of the study participants after explaining all aspects of the study in detail. The study was initiated only after obtaining approval from the Institutional Ethics Committee.

The study was conducted in accordance with the guidelines of the International Conference on Harmonisation – Good Clinical Practice (ICH-GCP). After obtaining written informed consent, febrile children admitted to the paediatric general ward were enrolled. Children admitted to the paediatric IPD were block-randomized into two groups based on the oral antipyretic administered and were observed for a period of 24 hours.

- Group A: Paracetamol at a dose of 10-15 mg/kg 6 hourly
- Group B: Mefenamic acid at a dose of 4-8 mg/kg 6 hourly

The following parameters were recorded in all the groups:

1. Evaluation of efficacy: By using an Omron® MC 246 Digital. Thermometer, Axillary temperature was recorded.
- The temperature was measured at: At the time of admission then after 1 hour, 4 hours and 6 hours then repeat the cycle for recording body temperature.

2. Withdrawal of the patient from the study:
- The patient condition deteriorates or becomes severely ill
- Withdrawal of consent of the parents/guardians.

3. Tolerability evaluation Modified treatment and tolerability evaluation score (MTTES) [11-14]:

Vomiting, dislikeness for meal, daytime sleep and additional medication were assessed and scores were recorded from 0-3 (absent – severe)

- Score 0: Absent – No symptoms.
- Score 1: Mild – Symptom is present but not annoying or troublesome.
- Score 2: Moderate – Symptom is frequently troublesome but not interfere with normal daily activity or sleep.
- Score 3: Severe – Symptom is sufficiently troublesome to interfere with normal daily activity or sleep.

Antipyretic effect evaluation:

Age, sex, weight, primary diagnosis, treatment received were recorded in Case Record Form for children attending pediatric out-patient department and presenting with fever as one of the presenting symptoms. Weight was measured using a calibrated weighing machine the participants, who fulfilled the inclusion criteria, were admitted to the pediatric ward. First group was received paracetamol 10-15mg/kg and second group received Mefenamic acid 4-8mg/kg, dose by oral route. Follow up of the patients were taken at intervals of 1 hour, 4-hour and 6-hour post dose by axillary thermometry till temp drops to normal range.

Results: -

A total of 120 febrile children were enrolled and analysed (Group A: Paracetamol, n = 60; Group B: Mefenamic acid, n = 60). Baseline demographic and anthropometric variables were comparable between groups (Table 1).

Antipyretic efficacy: -

Mean baseline and peak temperatures did not differ between groups, whereas the 1-hour post-dose temperature was lower with mefenamic acid (Table 2). Within-group reduction in temperature from baseline to 60 min was significant in both groups (Table 2).

Time to defervescence: -

The mean total time to reduce temperature to the normal range was shorter with mefenamic acid than with paracetamol (Table 3).

Next fever spike: -

Distribution of the next fever spike differed across time-windows between groups (Table 4).

Tolerability: -

Adverse events were infrequent and comparable between groups (Table 5).

Table 1. Baseline characteristics

Characteristic	Group A (Paracetamol) n=60	Group B (Mefenamic acid) n=60	P value
Age, years (mean ± SD)	5.84 ± 3.66	5.25 ± 3.37	0.3583
Age 1–5 y, n (%)	33 (55.0)	40 (66.66)	—
Age 5–10 y, n (%)	17 (28.33)	13 (21.66)	—
Age 10–14 y, n (%)	10 (16.66)	7 (11.66)	—
Male, n (%)	30 (50.0)	35 (58.33)	0.3596
Weight, kg (mean ± SD)	18.40 ± 11.47	16.67 ± 8.39	0.3457
Height, cm (mean ± SD)	104.22 ± 29.55	101.69 ± 25.25	0.6141
Religion—Hindu, n (%)	37 (61.66)	32 (53.33)	—
Religion—Muslim, n (%)	23 (38.33)	28 (46.66)	—

Table 2. Temperature outcomes

Outcome	Group A (Paracetamol) Mean ± SD	Group B (Mefenamic acid) Mean ± SD	P value
Baseline temperature, °F	100.66 ± 0.53	100.46 ± 0.50	0.9833
Peak temperature, °F	101.06 ± 0.70	101.04 ± 0.73	0.8783
Temperature at 1 hour, °F	99.62 ± 0.53	99.11 ± 0.59	<0.0001
Reduction 0–60 min, °F (within-group)	1.04 (p<0.0001)	1.35 (p<0.0001)	—

Table 3. Time to defervescence (minutes)

	Group A (Paracetamol)	Group B (Mefenamic acid)	P value
Total time to temperature reduction, min (mean ± SD)	85.95 ± 6.56	69.58 ± 6.39	<0.001

Table 4. Next fever spike—time window distribution

Time window for next spike	Group A n (%)	Group B n (%)	P value (overall)
No spike during observation	22 (36.66)	25 (41.66)	0.03638
1–5 hours	3 (5.0)	0 (0)	
6–10 hours	35 (58.33)	26 (43.33)	
>10 hours	0 (0)	9 (15.0)	

Table 5. Adverse events

Event	Group A n (%)	Group B n (%)	P value
Vomiting	0 (0)	1 (1.66)	0.3153
Dislikeness for meals	2 (3.33)	0 (0)	0.1538
Daytime sleeping	0 (0)	3 (5.0)	0.0794

Discussion: -

Fever, a common symptom in pediatric practice, is a physiological response mediated by pyrogenic cytokines, raising the hypothalamic set point and core body temperature [2,3]. While fever may aid in infection control, it can increase discomfort, risk of dehydration, febrile seizures, and metabolic complications, warranting antipyretic therapy to reduce morbidity in children [57,58]. Paracetamol remains the first-line antipyretic in children, supported by WHO recommendations, due to its efficacy, safety, and tolerability [59]. However, studies have shown that various NSAIDs, including mefenamic acid, exhibit effective antipyretic activity, with some reports suggesting superior efficacy compared to paracetamol [58,59]. The present prospective, comparative study assessed the efficacy

and tolerability of paracetamol versus mefenamic acid in febrile children over one year, with 120 participants equally divided into two groups. The mean time to reduce temperature was significantly shorter in the mefenamic acid group (69.58 ± 6.39 min) compared to the paracetamol group (85.95 ± 6.56 min) ($p \leq 0.001$). Additionally, the mean temperature reduction at 60 minutes was greater with mefenamic acid (1.35°F) than with paracetamol (1.04°F) ($p \leq 0.0001$), indicating superior rapid antipyretic action with mefenamic acid at 4–8 mg/kg/dose compared to paracetamol at 10–15 mg/kg/dose.These findings align with Kunkulol et al., who reported more effective temperature reduction with mefenamic acid within one hour [58]. Khubchandani et al. also found a greater drop in temperature with mefenamic acid (3.5°F) compared to paracetamol (2.44°F) and ibuprofen (2.79°F) over four hours [59]. The enhanced efficacy of mefenamic acid may be attributed to its central and peripheral COX inhibition, providing antipyretic, analgesic, and mild anti-inflammatory effects [51,52].

In contrast, some studies have reported that higher doses of paracetamol (15 mg/kg) provide better and sustained temperature reduction compared to lower doses (10 mg/kg) [49]. Additionally, ibuprofen has been shown to be marginally more effective than paracetamol in certain trials [62,63]. These findings highlight the importance of appropriate paracetamol dosing to ensure antipyretic efficacy while maintaining safety in children [49].In terms of safety, the current study found no significant difference in adverse effects between the two groups, with minimal occurrences of vomiting and no serious adverse events reported. These findings are consistent with Kunkulol et al., who reported good tolerability with both drugs [58]. Additionally, mefenamic acid delayed the next fever spike more effectively than paracetamol, potentially reducing the frequency of dosing and improving patient comfort.
Overall, the findings of this study support that while both paracetamol and mefenamic acid are effective in managing pediatric fever, mefenamic acid provides a faster reduction in temperature with comparable safety. This aligns with previous studies indicating that mefenamic acid may be considered when rapid defervescence is desired, particularly in cases where paracetamol is insufficient. However, careful monitoring is necessary due to the potential gastrointestinal and rare hematological side effects associated with NSAIDs, including mefenamic acid. Further large-scale studies assessing long-term outcomes and comparative safety profiles are recommended to guide rational antipyretic selection in pediatric practice.

Conclusion: -

This prospective, comparative study in febrile children found that mefenamic acid (4–8 mg/kg) reduced temperature more rapidly and sustained defervescence longer than paracetamol (10–15 mg/kg), with both drugs showing similar tolerability and minimal adverse effects. While mefenamic acid demonstrated superior efficacy, paracetamol remains a safe, cost-effective alternative for pediatric fever management. Both agents can be effectively used in clinical practice, with drug choice guided by efficacy, safety, and patient factors. However, limitations such as a small sample size and lack of drug level monitoring warrant larger, multi center studies with long-term follow-up to further evaluate the role of mefenamic acid in pediatric antipyresis.

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