The Antipyretic Effect of High-Dose Paracetamol Versus Mefenamic Acid in the Treatment of Febrile Children: A Randomized Controlled Trial

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Abstract

Fever is one of the most common symptoms leading to pediatric hospital visits, and effective antipyretic therapy is essential for symptom relief and prevention of febrile discomfort. Paracetamol and mefenamic acid are commonly prescribed antipyretics in India, yet comparative evidence on the efficacy of high-dose paracetamol versus mefenamic acid remains limited. This randomized controlled trial aimed to compare the antipyretic effectiveness and safety of high-dose paracetamol and mefenamic acid in febrile children. A total of 160 children aged 6 months to 12 years presenting with fever were randomized into two groups: Group A received paracetamol 15 mg/kg per dose, while Group B received mefenamic acid 5 mg/kg per dose. Axillary temperature was recorded at baseline and at 1, 2, 4, and 6 hours after drug administration. Primary outcome was reduction in body temperature, and secondary outcomes included time to defervescence and adverse effects. Both drugs produced significant temperature reduction, but high-dose paracetamol achieved faster and greater decline in temperature at early time points. Adverse effects were mild and comparable in both groups. The study demonstrates that high-dose paracetamol is at least as effective as mefenamic acid in reducing fever and may offer faster symptomatic relief with a favorable safety profile.

Keywords: Fever; Paracetamol; Mefenamic acid; Antipyretic; Pediatric randomized trial; Febrile children

Introduction

Fever is one of the most frequent clinical presentations in pediatric practice and is commonly associated with infectious illnesses in children [1]. Although fever itself is a physiological defense mechanism, it often causes discomfort, irritability, dehydration, and parental anxiety, leading to widespread use of antipyretic medications [2]. Effective fever control improves child comfort, feeding, and sleep, thereby supporting recovery and reducing unnecessary hospital visits [3]. Among available antipyretics, paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used in pediatric populations [4]. Paracetamol acts centrally by inhibiting prostaglandin synthesis in the hypothalamus, leading to reduction in the thermoregulatory set point, while NSAIDs such as mefenamic acid exert antipyretic effects through peripheral and central cyclooxygenase inhibition [5]. Paracetamol is widely considered first-line therapy due to its safety profile, whereas mefenamic acid is often used in older children for its combined analgesic and antipyretic properties [6]. In Indian clinical practice, mefenamic acid is frequently prescribed despite concerns regarding gastrointestinal and renal adverse effects associated with NSAIDs [7]. High-dose paracetamol within recommended therapeutic limits (15 mg/kg per dose) has been shown to provide more effective temperature reduction without increasing toxicity risk when dosing guidelines are followed [8]. However, comparative randomized studies between high-dose paracetamol and mefenamic acid in febrile children are limited, particularly in Indian hospital settings. Some studies suggest equivalent

antipyretic efficacy, while others report faster onset of action with paracetamol [9,10]. Considering the widespread and sometimes unsupervised use of antipyretics, evidence-based guidance is essential to ensure both effectiveness and safety. The present study was therefore designed to compare the **antipyretic efficacy and safety of high-dose paracetamol versus mefenamic acid** in febrile children using a randomized controlled trial design in a tertiary care teaching hospital.

Materials and Methods

This prospective randomized controlled trial was conducted in the Department of Pediatrics of a tertiary care teaching hospital in North India from January 2024 to December 2024. Children aged 6 months to 12 years presenting with axillary temperature ≥38.5°C due to presumed infectious causes were eligible for inclusion. Exclusion criteria included history of hypersensitivity to study drugs, hepatic or renal disease, dehydration, history of NSAID-induced gastritis, prior antipyretic intake within 6 hours, and requirement of immediate intravenous therapy. Sample size was calculated assuming a minimum detectable temperature difference of 0.3°C between groups with 80% power and 95% confidence, yielding a minimum of 72 patients per group; allowing for attrition, 160 children were enrolled and randomized equally into two groups using computer-generated random numbers. Group A received oral paracetamol at 15 mg/kg per dose, and Group B received oral mefenamic acid at 5 mg/kg per dose. Baseline axillary temperature was recorded using calibrated digital thermometers before drug administration. Subsequent temperature measurements were taken at 1 hour, 2 hours, 4 hours, and 6 hours post-dose. Primary outcome was mean reduction in temperature from baseline at each time interval. Secondary outcomes included time to defervescence (temperature <37.5°C) and incidence of adverse effects such as vomiting, abdominal pain, rash, or drowsiness. Parents were observed in the ward during the monitoring period. Data were entered into Microsoft Excel and analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using independent t-test, while categorical variables were analyzed using chi-square test. A p-value <0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was taken from parents or guardians prior to enrollment.

Results

A total of 160 children were enrolled, with 80 in each group. The mean age in Group A (paracetamol) was 4.8±2.6 years and in Group B (mefenamic acid) was 5.1±2.9 years, with no significant difference between groups (p=0.52). Baseline mean temperature was comparable in both groups.

Table 1. Baseline Characteristics of Study Participants (n=160)

Variable	Paracetamol Group (n=80)	Mefenamic Acid Group (n=80)	p-value
Mean age (years)	4.8 ± 2.6	5.1 ± 2.9	0.52
Male : Female	46 : 34	44 : 36	0.74
Baseline temperature (°C)	39.1 ± 0.4	39.0 ± 0.5	0.36

Both groups showed significant reduction in temperature over time, but Group A demonstrated greater reduction at early time points.

Table 2. Mean Temperature Reduction After Drug Administration (°C)

Time Interval	Paracetamol Group	Mefenamic Acid Group	p-value
1 hour	0.8 ± 0.3	0.5 ± 0.3	<0.001
2 hours	1.4 ± 0.4	1.1 ± 0.4	0.002
4 hours	1.9 ± 0.5	1.8 ± 0.5	0.18
6 hours	2.1 ± 0.6	2.0 ± 0.6	0.42

Time to defervescence was significantly shorter in the paracetamol group (2.6 ± 0.9 hours) compared to the mefenamic acid group (3.2 ± 1.1 hours), p=0.01. Adverse effects were mild and not significantly different between groups.

Table 3. Adverse Effects Observed in Both Groups

Adverse Effect	Paracetamol Group n (%)	Mefenamic Acid Group n (%)
Vomiting	4 (5.0)	6 (7.5)
Abdominal pain	2 (2.5)	5 (6.3)
Rash	1 (1.3)	1 (1.3)
Total	7 (8.8)	12 (15.0)

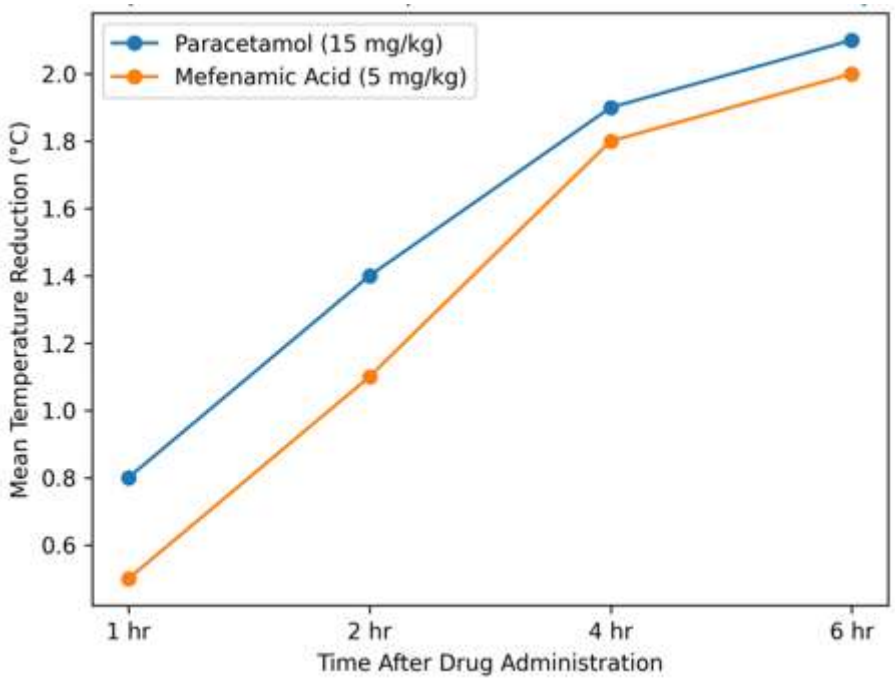

Figure 1. Comparison of Mean Temperature Reduction Between Groups Over Time

Discussion

The present randomized controlled trial demonstrates that **high-dose paracetamol provides faster and comparable overall antipyretic efficacy compared to mefenamic acid** in febrile children. Early temperature reduction at 1 and 2 hours was significantly greater in the paracetamol group, suggesting quicker onset of action. These findings are consistent with studies by Sarrell et al. and Perrott et al., which reported rapid central antipyretic effects of paracetamol due to hypothalamic prostaglandin inhibition [8,9]. Mefenamic acid showed effective fever reduction at later time points, indicating sustained antipyretic activity, but without superior efficacy. The shorter time to defervescence observed with paracetamol supports its role as first-line therapy in pediatric fever management. Safety analysis revealed fewer gastrointestinal complaints in the paracetamol group, aligning with known NSAID-related gastric irritation risks [7]. In Indian clinical practice, widespread use of mefenamic acid may be influenced by perception of stronger analgesic effect, yet evidence suggests no significant advantage over paracetamol for fever control alone. The findings support current pediatric guidelines that recommend paracetamol as the preferred antipyretic in children [4]. Limitations of the study include short follow-up duration and reliance on axillary temperature rather than core temperature measurement. Long-term safety outcomes and repeated dosing effects were not evaluated. Future studies may include ibuprofen as a comparator and assess comfort scores in addition to temperature reduction.

Conclusion

The study concludes that **high-dose paracetamol (15 mg/kg) is at least as effective and provides faster antipyretic action compared to mefenamic acid** in febrile children, with a favorable safety profile. Given its efficacy, safety, and guideline support, paracetamol should remain the first-line antipyretic agent in pediatric fever management. Routine use of mefenamic acid for uncomplicated fever may not offer additional benefit and should be reserved for specific clinical indications.

Ethical Approval

Ethical approval was obtained from the Institutional Ethics Committee of the institution prior to commencement of the study.

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