

Editorial

Treating a Fever

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INTRODUCTION

What is a fever? A fever is a controlled elevation of the body's temperature above the normal range of 98°F to 98.6°F (36.7°C to 37°C) [1]. According to the American Academy of Pediatrics (AAP), a temperature above 100.4°F (38°C) is what most pediatricians consider to be a sign of a fever [2]. Treatment is typically not required in a healthy child with a temperature below 102.2°F (39°C) [3]. However, parents will often treat a fever to return the child's temperature back to a normal temperature, but the goal of treating the fever should be to help the child's discomfort [4].

How parents measure the child's temperature can vary greatly and include measuring temperatures via the oral, rectal, axillary and tympanic routes. While the rectal temperature is usually the measurement considered to be as similar to the central temperature as possible, it is the most uncomfortable form of measurement for the child. The Italian Pediatric Society Guidelines recommends the axillary route to be utilized as the measurement of choice for parents or caregivers utilizing a digital thermometer [5]. The axillary route is well tolerated by the child, more easily to perform by parents and caregivers, and can be more accurate in a new born child than other routes [5].

Antipyretics

If a fever is measured, parents may administer an antipyretic to treat the fever including either acetaminophen or ibuprofen. Both antipyretics are widely used, although ibuprofen should not be used in children under 6 months of age. Acetaminophen, a para-aminophenol derivative, is readily available for administration via the oral and rectal routes of administration while ibuprofen, a propionic acid derivative, is only readily available to parents to be administered orally. Acetaminophen reaches peak plasma concentrations within 30 minutes with 2 hours being the time acetaminophen reaches maximal temperature reduction compared to ibuprofen which reaches peak plasma concentrations within 60 minutes and maximal temperature reduction in 3 hours [6]. Acetaminophen can be dosed every 4 to 6 hours with no more than 5 doses recommended in a 24 hour period compared to ibuprofen dosed every 6 to 8 hours (Table 1). Hepatotoxicity is of primary concern with chronic acetaminophen doses while nephrotoxicity concerns have been discussed with ibuprofen administration especially in situations with dehydration [4].

Clinical trials

Both acetaminophen and ibuprofen are effective for decreasing fevers, but the question still exists if one antipyretic is more efficacious than another. In a literature review conducted by Goldman et al. [8], various studies comparing acetaminophen and ibuprofen via single doses and multiple doses were evaluated. A few of the studies evaluated did show a slight advantage for ibuprofen over acetaminophen; however the authors indicated the comparisons were debatable due to methodological flaws. The authors concluded, in the end, that there was no significant advantage of one antipyretic over the other.

If one antipyretic is not more efficacious than the other, is a combination of therapy more effective for lowering a fever. In a prospective, randomized placebo controlled, double-blind study, Kramer et al. [9] compared the antipyretic efficacy of alternating acetaminophen with ibuprofen administered 3 hours apart when compared to two doses of acetaminophen administered 4 hours apart. No statistical difference was noted with the mean temperatures between the groups at hours 0, 3 and 6. A slight difference in mean temperature was observed in the acetaminophen alternated with ibuprofen group compared to the acetaminophen group at hour 4 with temperatures of 37.4°C (37.0°C-37.8°C) and 38.0°C (37.5°C-38.5°C), respectively ($P = 0.05$). A more significant difference was observed in the acetaminophen alternated with ibuprofen group compared to the acetaminophen group at hour 5 with temperatures of 37.1°C (36.8°C-37.4°C) and 37.9°C (37.5°C-38.3°C), respectively ($P = 0.003$). Although these results show that an alternative therapy may be more efficacious, it is not clear if these results are clinically significant. Even so, there still remains a concern about the safety of alternating regimen. In this study, parents primarily

Table 1: Antipyretic Dosing Recommendations [7].

Acetaminophen	Infants and Children up to 12 years of age: Oral: 10 to 15 mg/kg/dose every 4 to 6 hours Rectal: 10 to 20 mg/kg/dose every 4 to 6 hours (Not to exceed 5 doses in 24 hours)
Ibuprofen	Infants and Children 6 months to 12 years of age: Temperature < 102.5°F (39°C): 5 mg/kg/dose every 6 to 8 hours Temperature ≥ 102.5°F: 10 mg/kg/dose every 6 to 8 hours (Maximum daily dose of 40 mg/kg/day)

reported gastrointestinal symptoms; there was no difference in the occurrence of these symptoms between the groups.

Paul et al. [10] conducted a study comparing 3 different treatment regimens for the treatment of fever. Ibuprofen alone was compared to a combination of acetaminophen and ibuprofen administered together to Ibuprofen alternated with acetaminophen administered at 3 hours apart. The combination and alternating treatment arms had greater effects on temperature compared with the ibuprofen alone group at hour 4 36.9°C (0.3), 36.9°C (0.3), and 37.5°C (1.1), respectively ($P = 0.002$); hour 5 36.9°C (0.5), 36.8°C (0.3), and 38.0°C (1.1), respectively ($P < 0.001$); and hour 6 37.2°C (0.6), 36.9°C (0.3), and 38.5°C (1.5), respectively ($P < 0.001$). This study did not evaluate the effect of multiple doses over a longer period of time or adverse events that may occur with each regimen.

CONCLUSION

Even though alternative therapy was statistically significant, it is unsure if these results are clinically significant especially over a 24 hour period. There are concerns about adverse events with combined therapy, such as possible renal toxicity caused by the additive and maybe synergistic effects of the drug metabolites in children with dehydration [11]. Other issues to take into account include parental or caregiver confusion in regards to timing of each dose and the children may be mis-dosed [9]. If the clinician does not feel comfortable suggesting alternative dosing schedule to caregivers, then ibuprofen alone may be a viable option.

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REFERENCES

1. Lee GC, Burgess DS. Chapter 83. Antimicrobial Regimen Selection.

- In: DiPiro JT, Talbert RL, Yee GC, et al. Pharmacotherapy: A Pathophysiologic Approach. 9th ed. New York, NY: McGraw-Hill.
- American Academy of Pediatrics. Signs and Symptoms of Fever. Health Children website. Assessed January 27, 2013.
 - Powell KR. Chapter 174. Fever. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF. Nelson Textbook of Pediatrics. 18th ed. Philadelphia, PA: Saunders Elsevier.
 - Sullivan JE, Farrar HC. Clinical Report: Fever and Antipyretic Use in Children. American Academy of Pediatrics. 2011; 127: 580-587.
 - Chiappini E, Principi N, Longhi R, Tovo PA, Becherucci P, Bonsignori F, et al. Management of fever in children: summary of the Italian Pediatric Society guidelines. Clin Ther. 2009; 31: 1826-1843.
 - Sarrell E, Wielunsky E, Cohen H. Antipyretic Treatment in Young Children with Fever: Acetaminophen, Ibuprofen, or Both Alternating in a Randomized, Double-Blind Study. Archives of Pediatrics & Adolescent Medicine. February 2006; 160: 197-202.
 - Lexicomp. Pediatric and Neonatal Dosage Handbook. Assessed January 27, 2013.
 - Goldman R, Ko K, Linett L, Scolnik D. Antipyretic Efficacy and Safety of Ibuprofen and Acetaminophen in Children. The Annals of Pharmacotherapy. 2004; 38: 146-150.
 - Kramer L, Richards P, Thompson A, Harper D, Fairchok M. Alternating Antipyretics: Antipyretic Efficacy of Acetaminophen versus Acetaminophen alternated with Ibuprofen in Children. Clinical Pediatrics. 2008; 47: 907-911.
 - Paul IM, Sturgis SA, Yang C, Engle L, Watts H, Berlin CM Jr. Efficacy of standard doses of Ibuprofen alone, alternating, and combined with acetaminophen for the treatment of febrile children. Clin Ther. 2010; 32: 2433-2440.
 - Chiappini E, Venturini E, Principi N, Longhi R, Tovo PA, Becherucci P, et al. Update of the 2009 Italian Pediatric Society Guidelines about management of fever in children. Clin Ther. 2012; 34: 1648-1653.

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