

Ibuprofen was more protective against asthma morbidity than acetaminophen in asthmatic children with fever

Lesko SM, Louik C, Vezina RM, Mitchell AA. Asthma morbidity after the short-term use of ibuprofen in children. *Pediatrics*. 2002 Feb;109:e20.

QUESTION

In asthmatic children with a febrile illness, does ibuprofen increase asthma morbidity more than acetaminophen?

DESIGN

Subgroup analysis of a randomized {allocation concealed*}†, blinded (clinicians, patients, and {outcome assessors}†),* controlled trial with 1-month follow-up (Boston University Fever Study).

SETTING

Pediatric practices throughout the United States.

PATIENTS

1879 children between 6 months and 12 years of age (median age 46 mo, 62% boys) who were being treated for asthma with a β -agonist, theophylline, or inhaled steroid and had a febrile illness. Exclusion criteria were known sensitivity to acetaminophen, ibuprofen, aspirin, or any nonsteroidal anti-inflammatory drug (NSAID); nasal polyps; angioedema; or bronchospastic reactivity to aspirin or other NSAIDs. Follow-up was complete.

INTERVENTION

Patients were allocated to suspensions of ibuprofen, 5 mg/kg of body weight ($n = 636$); ibuprofen, 10 mg/kg ($n = 611$); or acetaminophen, 12 mg/kg ($n = 632$).

MAIN OUTCOME MEASURES

Morbidity from asthma: ≥ 1 hospitalization or outpatient visit within 1 month after enrollment.

MAIN RESULTS

18 patients were hospitalized during follow-up: 4, 6, and 8 patients in the ibuprofen 5 mg/kg, ibuprofen 10 mg/kg, and acetaminophen groups, respectively. The ibuprofen and acetaminophen groups did not differ for hospitalization for asthma (Table). Fewer patients who received ibuprofen had an outpatient visit for asthma than did patients who

received acetaminophen (Table). The risk for an outpatient visit did not vary by ibuprofen dose (5 vs 10 mg). Ibuprofen was most effective among children being treated for febrile illness caused by respiratory infections (relative risk 0.43, 95% CI 0.24 to 0.79).

CONCLUSION

In asthmatic children with a febrile illness, ibuprofen did not cause more asthma morbidity than did acetaminophen and reduced the number of outpatient visits.

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*See Glossary.

†Information provided by author.

Ibuprofen, 5 or 10 mg/kg of body weight, vs acetaminophen, 12 mg/kg, for febrile illness in children with asthma

Outcomes at 1 mo	Relative risk (95% CI)
≥ 1 hospitalization	0.63 (0.25 to 1.6)
≥ 1 outpatient visit	0.59 (0.37 to 0.93)
	0.56 (0.34 to 0.95)‡

‡Adjusted for age, sex, and race.

COMMENTARY

The large, randomized, double-blind, acetaminophen-controlled trial by Lesko and colleagues enrolled patients from > 2000 physicians' offices throughout the United States. Importantly, as noted in the original study, the antipyretics were indistinguishable with respect to color, flavor, and dosing schedule (1).

It is well-known that aspirin and other NSAIDs can precipitate bronchoconstriction in persons with asthma (2, 3). Reactions occur in 0.3% of the general population; in 10% of children with isolated asthma; and in 30% to 40% of persons with asthma, nasal polyposis, and chronic rhinosinusitis. Therefore, the authors excluded patients with known sensitivity to any NSAID.

Testing the hypothesis that ibuprofen might still increase morbidity, the results were surprising: Patients using ibuprofen had fewer outpatient visits for asthma. The 95% confidence interval excluded zero, and the relative risk for children with respiratory illness was even lower. The authors state that because airway inflammation is a feature of asthma, it is plausible that the anti-inflammatory effect of ibuprofen could offer some protection. Additionally, NSAIDs block the TH2 cytokine responses or allergic (IgE promoting) responses.

Although the number of visits according to antipyretic and dose was reported, the number of children was not. If by chance 1 group included a few children with an excessive number of visits (outliers), the results could be suspect. Of interest was that the antipyretics were used for such a short time. In the original study, the median number of doses was between 6 and 10 and the median duration of treatment was 3 days (1).

The results are encouraging. Further research is needed to confirm the results and to quantify the results with pulmonary function testing.

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References

1. Lesko SM, Mitchell AA. An assessment of the safety of pediatric ibuprofen: a practitioner-based randomized clinical trial. *JAMA*. 1995;273:929-33.
2. Szczeklik A. Antipyretic analgesics and the allergic patient. *Am J Med*. 1983;75:82-4.
3. Lumry WR, Curd JG, Stevenson DD. Aspirin-sensitive asthma and rhinosinusitis: current concepts and recent advances. *Ear Nose Throat J*. 1984; 63:66-74.