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


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

Design
Subgroup analysis of a randomised [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
1870 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 non-steroidal 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 admission to hospital or outpatient visit within 1 month after enrollment.

Main results
18 patients were admitted to hospital 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 hospitalisation for asthma. Fewer patients who received ibuprofen had an outpatient visit for asthma than did patients who received acetaminophen. The risk for an outpatient visit did not vary by ibuprofen dose (5 or 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).

Outcomes at 1 month

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative risk (95% CI)</th>
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<tr>
<td>≥1 admission to hospital</td>
<td>0.63 (0.25 to 1.6)</td>
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<tr>
<td>≥1 outpatient visit</td>
<td>0.59 (0.37 to 0.93)</td>
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<tr>
<td>1 outpatient visit</td>
<td>0.56 (0.34 to 0.96)†</td>
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†Adjusted for age, sex, and race.

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.

Commentary

The large, randomised, double-blind, acetaminophen-controlled trial by Lesko et al enrolled patients from >2000 physician’s offices throughout the United States. Importantly, as noted in the original study, the antipyretics were indistinguishable with respect to colour, flavour, and dosing schedule.1

It is well known that aspirin and other NSAIDs can precipitate bronchoconstriction in people with asthma.2–4 Reactions occur in 0.3% of the general population; in 10% of children with isolated asthma; and in 30% to 40% of people with asthma, nasal polypsis, 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.3

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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