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Acetaminophen-induced urticaria and tolerance of ibuprofen in an eight-year-old child

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NSAIDS Nonsteroidal antiinflammatory drugs

Acetaminophen is a widely used analgesic-antipyretic. Allergic-like adverse reactions to acetaminophen are rare; however, urticaria, bronchospasm, and life-threatening reactions have been reported.^{1,3} A clinically important question is whether persons with adverse reactions to acetaminophen can safely take other nonsteroidal antiinflammatory drugs (NSAIDs). This case illustrates acetaminophen-induced urticaria in a young girl who was subsequently able to tolerate ibuprofen.

An 8-year-old girl had two prior episodes of acute urticaria. The first episode occurred 4 weeks before evaluation. About 1 hour after ingesting two chewable acetaminophen tablets (Junior Strength Tylenol, 160 mg of acetaminophen per tablet, grape-flavored), the child complained of generalized itching, and several hives were present on her trunk. The symptoms resolved within an hour after oral administration of diphenhydramine.

The second episode occurred 3 weeks later. The child was given two chewable acetaminophen tablets, of the same brand, for treatment of a headache. About 90 minutes later, the child complained that her feet were itching. The mother noticed redness around the child's eyes, and over 30 minutes, hives developed on her face and trunk. The mother did not notice any other symptoms. The symptoms again resolved after oral administration of diphenhydramine.

The child's medical history was unremarkable. There was a history of asthma and allergic rhinitis in the father.

Results of physical examination were unremarkable, including normal appearing skin and no evidence of dermatographism.

During the evaluation, the child was orally challenged with the same brand of chewable acetaminophen tablets, starting with one half tablet; then a second half tablet and a full tablet were given at 30-minute intervals. Approximately 90 minutes after the last dose, the child had generalized pruritus and 10 to 15 small (average, 0.5 to 1.5 cm), urticarial lesions on the trunk and face. She had no other symptoms.

A second oral challenge was performed 2 weeks after the initial challenge to determine whether the reactions were related to the flavorings and dyes in the chewable tablets or to the acetaminophen. The child had not had any urticaria during the interval. A single, nonchewable, 325 mg acetaminophen tablet (regular-strength Tylenol) was used. Fifteen minutes later, the child had intense generalized pruritus; 10 to 20 small urticarial lesions on the trunk, neck and face; and mild swelling around the eyes. She was treated with 0.2 ml of aqueous epinephrine and 25 mg of oral diphenhydramine with prompt resolution of symptoms. No wheezing or shortness of breath was observed, and her blood pressure remained stable.

The mother was very concerned that she would not be able to treat the child for headaches or fever because she had been advised to have the child avoid all NSAIDs. After consultations concerning adverse reactions to NSAIDs, a third challenge was undertaken. The potential benefits and risks were extensively discussed with the mother and child. Ibuprofen suspension (100 mg/5 ml, Children's Motrin) was chosen as the preferred agent because ibuprofen would be a reasonable alternative to acetaminophen, if it could be tolerated. Doses of 20, 40, 80, and 160 mg were given at 90-minute intervals for a total dose of 300 mg or 9.7 mg/kg of body weight. The child did not have any symptoms during or after the challenge.

To evaluate the possibility that the urticaria was related to IgE antibodies, the chewable and plain acetaminophen tablets were dissolved in sterile buffered saline with phenol, yielding solutions with concentrations of 35.6 and 36.1 mg/ml acetaminophen, respectively. Because no reports of positive skin test responses to acetaminophen could be found, these concentrations were arbitrarily chosen

after considering the negative results reported by other investigators with a concentration of 5 mg/ml.³ After the solutions were sterile-filtered, the child was skin tested by the prick technique with the two acetaminophen solutions, 1 mg/ml histamine, and buffered saline. There was no response to either of the acetaminophen solutions and a normal positive response to the histamine (wheal 5 × 6 mm with surrounding flare).

The child has been followed up for 1 year, and during this time she has received ibuprofen on several occasions without difficulty.

Discussion

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This case illustrates that acetaminophen can produce acute urticaria even in young children and that the presence of urticaria after administration of acetaminophen does not indicate a risk of adverse reactions to all other NSAIDs. Although urticaria caused by acetaminophen has rarely been reported, it is impossible to know whether such reactions are truly rare or are often incorrectly attributed to other causes, such as antibiotics, in ill children.¹⁻³

Without multiple challenges it is impossible to be absolutely sure that an excipient in the acetaminophen preparations did not cause the observed urticarial reactions, but according to the *Physicians' Desk Reference*, the only excipient common to both the grape-flavored and regular-strength acetaminophen tablets is magnesium stearate.⁴ No flavorings or dyes are listed for the regular-strength tablet. The tolerated ibuprofen preparation does have citric acid and cornstarch in common with the grape-flavored acetaminophen, but the dyes are different and the flavorings are not specifically identified.⁴

The most important clinical question in the treatment of this child was the risk of adverse reactions to other NSAIDs after her sensitivity to acetaminophen was known.⁵ Adverse reactions to NSAIDs are usually thought to result from cyclooxygenase inhibition. Because acetaminophen minimally inhibits cyclooxygenase, it is usually considered safe for persons sensitive to NSAIDs. Previous studies relating adverse reactions to acetaminophen and other NSAIDs have yielded conflicting results.⁵⁻⁷ Falliers⁶ did not find any reactivity to acetaminophen in 15 aspirin-sensitive adults challenged with a cumulative dose of 2005 mg of acetaminophen. In contrast, Delaney⁷ reported that 12 of 42 adult patients with asthma and aspirin sensitivity responded to acetaminophen.

Settipane and Stevenson⁵ documented a fall of greater than 20% in FEV₁ after administration of 1000 mg of acetaminophen in three aspirin-sensitive adults with histories of reactions to acetaminophen. Aspirin desensitization was attempted in two patients, and after aspirin desensitization, both patients were able to tolerate 1000 mg of acetaminophen. Settipane and Stevenson⁵ claimed that these cases documented cross-sensitivity between acetaminophen and aspirin. In contrast, Ellis et al.³ described two children with asthma who experienced bronchospasm within 15 minutes of receiving acetaminophen but who tolerated aspirin.

In this case the sensitivity to acetaminophen did not appear to be due to inhibition of

cyclooxygenase because ibuprofen is a more potent inhibitor than acetaminophen. An IgE-mediated mechanism seems unlikely because results of skin tests with relatively concentrated solutions of the offending preparations were negative, but the true value of skin testing will remain unknown until dose-response studies have been performed on individuals with positive skin test results. It is impossible to know whether the current case represents a unique mechanism until additional cases have been similarly evaluated.

References

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1. Cole FOA. Urticaria from paracetamol [letter]. Clin Exp Dermatol 1985;10:404.

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2. Doan T, Greenberger PA. Nearly fatal episodes of hypotension, flushing, and dyspnea in a 47-year-old woman. Ann Allergy 1993;70:439-44.

[MEDLINE](#)

3. Ellis M, Haydik I, Gillman S, Cummins L, Cairo, MS. Immediate adverse reactions to acetaminophen in children: evaluation of histamine release and spirometry. J Pediatr 1989;114:654-6.

4. Physicians' Desk Reference. 50th ed. Montvale (NJ): Medical Economics Co., 1996:1546,1557-8.

5. Settipane RA, Stevenson DD. Cross sensitivity with acetaminophen in aspirin-sensitive subjects with asthma. J Allergy Clin Immunol 1989;84:26-33.

[MEDLINE](#)

6. Falliers CJ. Acetaminophen and aspirin challenges in subgroups of asthmatics. J Asthma 1983;20(S-1):39-49.

[MEDLINE](#)

7. Delaney JC. The diagnosis of aspirin idiosyncrasy by analgesic challenge. Clin Allergy 1976;6:177-81.

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