Infant Acetaminophen Use Tied to Asthma Later

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Exposure to acetaminophen may be an important risk factor for the development of asthma later in childhood, according to new data from an international asthma study.

In a sample of more than 200,000 children from 31 countries, those children given acetaminophen—known outside the United States as paracetamol—for fever during their first year of life were approximately 50% more likely to have experienced asthma symptoms at age 6-7 years than were unexposed children. Dr. Richard Beasley of the Medical Research Institute of New Zealand, Wellington, and his colleagues reported that in phase III of the International Study of Asthma and Allergies in Childhood (ISAAC), exposure to acetaminophen in the first year of life was associated with significantly increased risk of severe asthma symptoms, as well as rhinoconjunctivitis and eczema at 6-7 years (Lancet 2008;372:1039-48).

The prevalence of asthma has increased substantially over the past 50 years, as has the use of acetaminophen in children, the authors wrote. Previous studies have reported associations between asthma risk and exposure to acetaminophen in utero, during infancy, and in late childhood and adulthood in populations from developed and developing countries. Additionally, phase I of ISAAC identified positive associations between per-person acetaminophen consumption and asthma prevalence in children, they stated.

The current analysis was designed to evaluate the consistency of the association between acetaminophen and asthma and to investigate one of the proposed biological mechanisms for the link—specifically, that acetaminophen exposure contributes to the development of oxidant-induced airway inflammation caused by reduced concentrations of the antioxidant glutathione in the lung and stimulation of the T helper cell 2 response.

Toward this end, parents and guardians of 205,487 children aged 6-7 years from 73 centers were asked to complete two standardized questionnaires, including a prevalence questionnaire about symptoms of asthma, rhinoconjunctivitis, and eczema, and an environmental questionnaire about possible protective and risk factors for asthma and allergic disorders including the use of acetaminophen in the first year of life and now.

The primary outcome measure for the analysis was the association between acetaminophen use for fever in the first year of life and asthma symptoms at 6-7 years as measured by multivariate analysis.

A total of 194,555 children were included in the analysis of acetaminophen use for fever during the first year of life. Of these, 105,041 had complete covariate data and were included in the multivariate analysis. In this group, the association between asthma symptoms and acetaminophen use in the first year of life was significant (odds ratio 1.46). Similarly, the association between first year acetaminophen use and rhinoconjunctivitis and eczema were significant (OR 1.48 and 1.35, respectively).

Despite the study's power, size, and multinational nature, the findings do not establish causality because of its design, the authors stressed. In the absence of an adequately powered, population-based randomized control trial, "evidence is insufficient to advise parents and health care workers of the risk benefit of taking [acetaminophen] in childhood, or its comparative efficacy and safety with other approaches," they wrote.

In an accompanying editorial, Dr. R. Graham Barr of Columbia University Medical Center, New York, agreed. "The studies to date are suggestive but not definitive enough to recommend a wholesale change in antipyretic use in children. Acetaminophen has known benefits for pediatric febrile illness as well as known toxicities," he wrote. "The drug might contribute to asthma incidence and it might be prudent to minimize casual use of this—and all—drugs in otherwise healthy children. However, we need to take the guesswork out of recommending and prescribing antipyretic drugs for children." What is needed, he wrote, are randomized trials that examine the incidence of childhood asthma, comparing acetaminophen use with an active control such as ibuprofen or placebo (Lancet 2008;372:1011-2). Dr. Beasley reported having received grant support and honoraria for lectures from GlaxoSmithKline Inc., the maker of acetaminophen. ■

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