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Sanjay Gupta, MD, Editor

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Acetaminophen Found Safe for Kids With Asthma

— No extra risk for exacerbations vs ibuprofen

by Molly Walker
Staff Writer, MedPage Today

Acetaminophen did not increase the rates of asthma attacks among young children with mild asthma who were given the drug to reduce fever or pain when compared with ibuprofen, a small randomized trial found.

Among participants, ages 12 months to 59 months, who received a median of 5.5 doses (interquartile range, 1.0 to 15.0) of trial medication, there were no differences in the rates of asthma attacks between groups of children with mild, persistent asthma who were given either acetaminophen or ibuprofen on an as-needed basis for fever or discomfort,

reported William J. Sheehan, MD, of Boston Children's Hospital, and colleagues, as part of the National Heart, Lung, and Blood Institute's (NHLBI) Asthma Network (AsthmaNet).

Similarly, there were no differences between groups of children in the percentage of

asthma-control days, times when children needed a rescue inhaler, or unscheduled healthcare visits relating to exacerbation of asthma, they wrote in the *New England Journal of Medicine*.

Co-author Wanda Phipatanakul, MD, also of Boston Children's Hospital, told *MedPage Today* in an email these results were reassuring, but not necessarily surprising.

"There was enough 'smoke' from observational data that our study aimed to test whether there truly was a cause for concern in a prospective, randomized, blinded clinical trial," she said.

Prior research in both children and adults has suggested a link between acetaminophen use among people with asthma and decreased lung function, with Sheehan's group adding that "some physicians have recommended that until data supporting its safety become available, acetaminophen should be completely avoided in children with asthma."

In an accompanying editorial, Augusto Litonjua, MD, MPH, of Brigham and Women's Hospital in Boston, characterized these findings as "the best answer we can get in this age group." But because a study with a placebo group would be unethical, there are some questions left unanswered by the study, she cautioned.

"The ... trial does not directly answer the question of whether the use of acetaminophen or ibuprofen, as compared with no drug use, can worsen asthma," Litonjua wrote. "The ... trial did not address whether acetaminophen use can lead to the development of asthma in otherwise healthy children; a different study will have to be designed to answer that question."

The current Acetaminophen versus Ibuprofen in Children with Asthma (ACIVA) trial randomized 300 children with mild, persistent asthma to receive either acetaminophen or ibuprofen for fever or pain when needed over the course of 4 months (48 weeks). Mean age at enrollment was 39.9 months.

Eighty percent of the participants used the medication at least once. Increased use of medication was significantly associated with number of asthma exacerbations, though there were no significant differences between groups.

Overall, 226 children completed the trial, but the researchers did not find significant differences either in the rate of exacerbations between groups when examining only this

population, or differences when examining the 200 children who both completed the trial and received at least one dose of medication.

The authors reported that, overall, there was a non-significant difference in asthma

exacerbations -- defined as requiring treatment with glucosteroids -- between the acetaminophen group (0.81 per participant over 46 weeks) and the ibuprofen group (0.87 per participant, RR 0.94, 95% CI 0.69 to 1.28). However, the authors noted there was "uncertainty" in this finding due to the wide confidence interval.

Secondary outcomes were similar, with no significant differences in asthma control days (85.8% in the acetaminophen group versus 86.8% in ibuprofen group), use of an albuterol rescue inhaler (2.8 versus 3.0 inhalations per week, respectively), and unscheduled healthcare utilization for asthma (0.75 and 0.76 episodes, respectively).

There were six serious adverse events in the acetaminophen group and 12 in the ibuprofen group, though there were no deaths during the trial.

Phipatanakul said that the results of this study had the potential to impact clinical practice, depending on if pediatricians were avoiding recommendations of acetaminophen based on the results of certain observational studies and editorials.

"If the answer is 'yes,' then this study may be reassuring that it is okay to use either Tylenol or Motrin in their young patients with asthma. If the answer is 'no,' then hopefully this study provides some added assurance," she said.

Limitations to the study included that the results may not be generalizable to children with more severe asthma and that the study does not answer the question of whether prenatal exposure to acetaminophen or exposure during the first year of life may be linked to the development of asthma.

But Phipatanakul characterized a pregnancy birth cohort trial comparing the two agents as "nearly impossible," and suggested other avenues for additional research.

"Future studies in older children or more severe asthmatics may be helpful," she said.

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Sheehan and Phipatanakul disclosed no relevant relationships with industry. Some co-authors disclosed relevant relationships with GlaxoSmithKline, Merck, Boehringer Ingelheim, Teva, Sunovation, Pfizer, McNeil Consumer Healthcare, the Consumer Healthcare Product Associations, Perrigo Nutritionals, Procter & Gamble,

Genentech, Novartis, Roche, Aerocrine, Vectura, Sanofi, DBV Technologies, Schering, TevaSepracor, SA Boney and Associates, Gilead Sciences, Nivalis Therapeutics, Celtaxsys, Insmed, Corbus, KaloBias, N30 Pharmaceuticals, Greer, Mylan, Philips Respironics, Regeneron, Cowen and Company, Array Biopharma, Ono

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Litonjua disclosed relevant relationships with UpToDate, Springer Humana Press, and AstraZeneca.

Reviewed by Robert Jasmer, MD *Associate Clinical Professor of Medicine, University of California, San Francisco and Dorothy Caputo, MA, BSN, RN, Nurse Planner*

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