Acid reflux drug does not improve asthma in children

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Children without symptoms of gastroesophageal reflux whose asthma was being poorly controlled with anti-inflammatory treatment did not have an improvement in symptoms or lung function with the added treatment of the proton pump inhibitor lansoprazole, compared to patients who received placebo, according to a study in the January 25 issue of *JAMA*. Use of lansoprazole was associated with increased adverse events.

"Asthma and gastroesophageal reflux (GER) disease are both common disorders in children, and symptoms of GER are frequently reported among children with asthma," according to background information in the article. "Untreated GER has been postulated to be a cause of inadequate asthma control in children despite inhaled corticosteroid treatment, but it is not known whether treatment with proton pump inhibitors improves asthma control."

Janet T. Holbrook, M.P.H., Ph.D., of the Johns Hopkins Bloomberg School of Public Health, Baltimore, and colleagues with the Writing Committee for the American Lung Association Asthma Clinical Research Centers, conducted a randomized, placebo-controlled clinical trial to compare the PPI lansoprazole with placebo in children with poor asthma control who were receiving inhaled corticosteroid treatment. The study included 306 participants, enrolled from April 2007 to September 2010 at 19 U.S. academic clinical centers, who were followed up for 24 weeks. A subgroup had an esophageal pH (a test for GER) study before randomization. Children were randomly assigned to receive either

lansoprazole (n=149) or placebo (n=157). The primary measured outcome was change in Asthma Control Questionnaire (ACQ) score (range, 0-6; a 0.5-unit change is considered clinically meaningful). Secondary outcome measures included lung function measures, asthma-related quality of life, and episodes of poor asthma control. The average age of the children was 11 years; there were more boys than girls, and 50 percent of participants were black.

The researchers found that after randomization, the ACQ score decreased by less than the meaningful clinically important difference in both groups; the change was not statistically different between treatment groups. There were no statistically significant treatment effects for any of the secondary outcomes.

Among the 115 children with adequate 24-hour esophageal monitoring studies, 43 percent (n = 49) had positive results for GER. In children with GER, there was no significant effect of lansoprazole treatment on any of the study outcomes, including asthma-related quality of life or lung function.

Of the participants, 10 in the lansoprazole group and 9 in the placebo group had 1 or more serious adverse events. The most common serious adverse event in both groups was asthma exacerbation (15 of 25 reports). Treatment with lansoprazole was associated with a greater prevalence of upper respiratory tract infections, sore throats, and episodes of bronchitis. "Our study raises important questions about adverse effects of lansoprazole treatment of children with asthma," the authors write.

"In conclusion, the results of our study indicate that PPI treatment of children with poorly controlled asthma without symptomatic GER was not an effective therapy for asthma and there may be significant safety concerns for long-term PPI use in children that warrant further study."

In an accompanying editorial, Fernando D. Martinez, M.D., of the University of Arizona, Tucson, writes that the "overuse of PPIs in childhood asthma and in pediatrics in general is another example of a subtle but frequent phenomenon in clinical practice: therapeutic creep."

"Clinicians extend the use of a treatment with real or suggestive therapeutic effects observed in a certain age group or in patients with a certain disease phenotype to other patients in whom the efficacy has never been demonstrated," Dr. Martinez writes. "Therapeutic creep increases the risk of potential adverse effects without any added advantage for patients. It is also plausible to surmise that this phenomenon has substantially contributed to the marked increase in asthma drug costs, which are now the largest component of the direct costs for the disease."

More information: *JAMA*. 2012;307[4]:373-381.
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