Pediatric Academic Societies Meeting

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# Study Finds Infants Prescribed Antacids for Reflux Have Increased Risk of Bone Fractures During Childhood

*Research suggests antacid medications should be used only be used for more severe symptomatic gastroesophageal reflux disease.*

SAN FRANCISCO – New research being presented at the 2017 Pediatric Academic Societies Meeting found infants prescribed antacids to manage acid reflux, or spitting up, under age 1 had more bone fractures later in childhood.

An abstract of the study, "Early Antacid Exposure Increases Fracture Risk in Young Children," will be presented on Sunday, May 7, at the Moscone West Convention Center in San Francisco.

Acid reflux, also known as gastro-esophageal reflux (GER), is frequently treated with drugs such as proton pump inhibitors (PPIs) and histamine H2-receptor antagonists (H2-blockers) that decrease production of stomach acids. These types of medications have been linked with increased bone fractures in adults, but there has been a lack of research into whether they might have the same effect in children.

Researchers examined the records of 874,447 healthy children born within the Military Healthcare System (MHS) from 2001 to 2013 who received care within the system for at least 2 years. They found approximately 10 percent of the children were prescribed antacids in the first year of life, including H2-blockers such as ranitidine (Zantac) and famotidine (Pepsid) as well as PPIs such as omeprazole (Prilosec) and pantoprazole (Protonix). A small percentage was prescribed both.

Children who used PPIs had a 22 percent increased likelihood of fracture, while children who used both PPIs and H2-blockers had a 31 percent increased likelihood of fracture. Use of H2-blockers was not associated with an immediate increase in factures, the study found, but there was an increased likelihood of fracture with time.

In addition, the number of bone fractures children experienced increased with the number of days they took these medications. The younger a child first began using antacid medications, the higher the fracture risk. Those started on antacid medications earlier--under 6 months old--had the most increased fracture risk. Children who started using antacids after age 2 years did not have increased fractures as compared to children who were not prescribed antacids in the first five years of life.

Use of antacid medications in infants should be weighed carefully against possible fracture, said U.S. Air Force Capt. Laura Malchodi, MD, lead author of the study and a pediatrics resident at Walter Reed National Military Medical Center.

"With many antacids easily available over-the-counter for adults, these medications may seem benign," Dr. Malchodi said. "However, our study adds to a growing body of evidence suggesting antacid medications are not safe for children, especially very young children, and should only be prescribed to treat confirmed serious cases of more severe symptomatic gastroesophageal reflux disease (GERD), and for the shortest length of time needed."

GER is a common condition that affects roughly 40 to 65 percent of all infants. It usually begins at approximately 2 to 3 weeks of life and peaks between 4 to 5 months. In most babies, GER disappears by about 1 year of age as the upper digestive tract functionally matures. The American Academy of Pediatrics believes it is important for all pediatric health care providers to be able to properly identify and treat children with reflux symptoms, and to distinguish GER from more worrisome disorders so as to avoid unnecessary treatments.

Dr. Malchodi will present the abstract, "Early Antacid Exposure Increases Fracture Risk in Young Children," at 11:45 a.m.

Reporters interested in an interview with U.S. Air Force Capt. Laura Malchodi, MD, may contact Sharon Holland with Uniformed Services University Public Relations at 301-295-3578.

*Please note: only the abstract is being presented at the meeting. In some cases, the researcher may have more data available to share with media, or may be preparing a longer article for submission to a journal. Contact the researcher for more information.*

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*The Pediatric Academic Societies (PAS) Meeting brings together thousands of individuals united by a common mission: to improve child health and wellbeing worldwide. This international gathering includes pediatric researchers, leaders in academic pediatrics, experts in child health, and practitioners. The PAS Meeting is produced through a partnership of four organizations leading the advancement of pediatric research and child advocacy: Academic Pediatric Association, American Academy of Pediatrics, American Pediatric Society, and Society for Pediatric Research. For more information, visit the PAS Meeting online at www.pas-meeting.org, follow us on Twitter @PASMeeting and #pasm17, or like us on Facebook.*

**ABSTRACT**

**TITLE**: Early Antacid Exposure Increases Fracture Risk in Young Children

**Background:** Antacids, including proton pump inhibitors (PPIs) and histamine H2-receptor antagonists (H2RAs) are frequently prescribed to treat gastro-esophageal reflux (GER) in healthy infants.[o1] PPI use [HE2] has been associated with increased fracture risk in older adults, the impact of PPI on fracture in children is unknown.

**Objective:** To examine the impact of antacid use during the first 6 months of life on infant and early childhood fracture

**Design/Methods:** We performed a retrospective cohort study of healthy children born within the Military Healthcare System (MHS) from 2001 to 2013 who received MHS care for two or more years. Outpatient pharmacy data identified prescriptions for PPIs and H2RAs during the first 6 months of life. International Classification of Disease 9th edition (ICD-9) codes identified fractures after 6 months of age. Children with diagnosed osteogenesis imperfecta, pathologic fractures, child maltreatment and a NICU stay of 7+ days were excluded; infants admitted to the NICU often use inpatient antacids, and inpatient prescription data was not available. Groups were compared using Wilcoxon rank-sum test and $\chi 2$ analysis. A Cox proportional hazard model assessed the relative hazard of fracture; adjusted analysis controlled for gender, prematurity, and low birth weight.

**Results:** 874,447[KW1] infants were born within the MHS between 2001 and 2013 and followed for two years or more (median 5.8, IQR 3.6-9.1 years). In the first 6 months of life 6,943 (0.8%) infants were prescribed PPIs, 67,096 (7.7%) H2RAs and 10,777 (1.2%) both. The median age at first antacid prescription was 2.9 months, PPI 3.5 months, and H2RA 3.0 months. Infants [LM2] who took antacids differed from controls on demographic and birth characteristics (Table 1). Fracture hazard was increased with male sex, PPI use, and use of both H2RAs and PPIs. Prior H2RA use alone was not associated with fracture, but interacted with time with fracture risk increasing with time. Fracture hazard was decreased with LBW and was not associated with preterm birth (Table 2, Figure 1).

**Conclusion(s):** Use of H2RAs and PPIs in infancy is associated with an increased hazard of childhood fracture in healthy children. Use of antacid medications in infants should be weighed carefully against possible fracture.