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**Pediatric PPI Use and Fractures**

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OBJECTIVES AND STUDY: Proton pump inhibitors (PPI) are one of the most widely prescribed classes of medications for pediatric and adult patients. In the last decade there are increasing reports of safety concerns regarding PPI use including the risk of fractures. Among the pediatric population, fractures represent a commonly encountered pathology and are associated with significant morbidity and economic burden. Few studies have evaluated PPI use and fracture risk among pediatric patients. We performed a retrospective propensity-matched analysis to compare the rate of fracture among pediatric patients prescribed PPI with those patients who did not receive PPI.

METHODS: Initial encounters for patients 6 months to 15.5 years were identified between 06/01/2011 to 12/31/2015 in the Pediatric Hospital Information System (PHIS) database, a database with encounters from 49 children’s hospitals in the United States. Encounters for patients outside the stated age range, encounters related to chronic illnesses, and encounters for patients with conditions or medications predisposing to fracture were excluded. Encounters were classified as PPI encounters if a charge for PPI was documented in the billing record. PPI encounters were propensity matched to non-PPI encounters on the basis of hospital, age, race, sex, payer, encounter type, median household income quartile, intensity of resource utilization and 3M’s All Patient Refined Diagnostic Related Group. Following initial encounter, patients were evaluated over a 2-year period for hospitalizations resulting from fracture. Categorical variables for PPI encounters and non-PPI encounters were compared using a Chi-square test. Continuous variables were compared using Wilcoxon rank-sum test.

RESULTS: Data from 32,001 healthcare encounters with documentation of PPI use were propensity matched to the same number of encounters with no documentation of PPI use. PPI encounters had median age of 4 years with a distribution of 0 to 3 years (48.8%), 4 to 8 years (15.2%), 9 to 13 years (23.9%), and greater than 14 years of age (12.1%). 48.5% of the PPI cohort was female. We found a statistically significant higher rate of fractures among the PPI exposed group (1.4% vs 1.2%, p = 0.019). Adjusting for remaining differences in sex, race, encounter type, payer, and resource intensity after matching, the difference remained statistically significant (p = 0.017) with an adjusted odds ratio (95% confidence interval) of 1.2 (1.0,1.4). Among all patients with fractures, upper extremity was the most common location, however the PPI cohort was more likely to suffer from lower extremity, rib, and spinal fracture compared to the control group (p = 0.01). We found no
relationship between fracture risk and individual proton pump inhibitors (p = 0.205).

CONCLUSIONS: This study suggests an increased risk of fracture among otherwise healthy pediatric patients taking PPI. Among patients hospitalized with a fracture, those documented as being prescribed PPI had a higher rate of lower extremity, rib, and spine fractures compared to controls and appeared to be a class effect not related to individual PPI agent. Future studies capturing data on duration of use, dosage, and mechanism are needed to further evaluate this relationship.