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Press Release

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CERTAIN REFLUX AND ULCER MEDICATIONS LINKED WITH BONE FRACTURES IN DIALYSIS PATIENTS

Highlights

- Among patients with kidney failure on dialysis, use of proton pump inhibitors was associated with a 19% higher risk of hip fracture. The association remained within subgroups of low, moderate, and high use, yielding of 16%, 21%, and 19% greater risks, respectively.
- Histamine-2 receptor antagonists were not associated with hip fracture events.

Washington, DC (September 27, 2018) — Certain medications commonly used to treat heartburn, acid reflux, and ulcers are linked with higher bone fracture risks among patients on dialysis, according to a new study. Almost three-quarters of patients who had a hip fracture had used the medications in the 3 years preceding their event. The findings appear in an upcoming issue of the *Clinical Journal of the American Society of Nephrology* (*CJASN*).

Among patients who have end-stage kidney disease, or kidney failure, and are on hemodialysis, hip fracture risk is estimated to be 4 times higher than in the general population. Many patients with kidney failure take medications called proton pump inhibitors (PPIs), which reduce stomach acid production and have been linked with hip fractures in the general population. Theoretically, histamine-2 receptor antagonists, which also reduce gastric acid production, would yield a similar association with hip fracture events if the mechanism of proposed risk involved acid suppression alone. Yet, studies in the general population conflict on whether these drugs are also linked with fractures.

To examine potential associations in patients with kidney failure, a team led by Chandan Vangala, MD and Wolfgang Winkelmayer, MD, PhD, ScD (Baylor College of Medicine) analyzed information from the US Renal Data System (USRDS) to identify all hip fracture events recorded between 2009 and 2014 among hemodialysis-dependent patients. All cases were matched with 10 patients on dialysis who did not experience hip fractures. Prescription drug information for the preceding 3 years was gathered from Medicare Part D claims.

In the analysis of 4551 hip fracture cases and 45,510 controls, a larger proportion of cases had any prior use of PPIs (70% vs. 63%) or histamine-2 receptor antagonists (25%

vs. 23%). After adjustments, use of PPIs was associated with a 19% higher risk of hip fracture. The association remained within subgroups of low, moderate, and high PPI use, yielding of 16%, 21%, and 19% greater risks, respectively. Histamine-2 receptor antagonists were not associated with hip fracture events.

“Proton pump inhibitors are the sixth most common type of medication prescribed among patients who are dependent on dialysis; however, their use is associated with increased hip fracture risk. Therefore, we recommend interval assessment of continued PPI use in hemodialysis-dependent patients, who already experience tremendous medication burden,” said Dr. Vangala.

In an accompanying editorial, Benjamin Lazarus, MBBS and Morgan Grams, MD, PhD (Johns Hopkins Bloomberg School of Public Health) noted that the association between PPI use and hip fracture is biologically plausible, but the observational study cannot definitively assert that PPI use causes hip fracture. “However, a randomized controlled trial to address risks of PPI use in patients receiving hemodialysis is probably not practicable,” they wrote. “Based on the available data, we suggest that PPI use in hemodialysis patients be individualized, with discontinuation as soon as medically indicated, and that patients are counseled about possible adverse effects, including the possibility of heightened risk of hip fracture.”

Study co-authors include Jingbo Niu, MD, DSc, Colin Lenihan, MB BCh BAO, PhD, William Mitch, MD, and Sankar Navaneethan, MD, MS, MPH.

Disclosures: Dr. Winkelmayer reports having served as an advisor or consultant, unrelated to the topic of this manuscript, to Akebia, Amgen, Astra-Zeneca, Bayer, Daichii-Sankyo, Relypsa, Vifor-Fresenius Medical Care Renal Pharma, and ZS Pharma. Dr. Navaneethan serves on the independent event adjudication committee for clinical trials sponsored by Bayer and Boehringer Ingelheim (unrelated to the topic of this manuscript). All other authors have no financial disclosures to report.

The article, entitled “Proton Pump Inhibitors, But Not Histamine-2 Receptor Antagonists, Associate with Hip Fracture Risk Among Patients on Hemodialysis,” will appear online at http://cjasn.asnjournals.org/ on September 27, 2018, doi:10.2215/CJN.02190218

The editorial, entitled “Proton Pump Inhibitors in Kidney Disease,” will appear online at http://cjasn.asnjournals.org/ on September 27, 2018.

any drug, changing your diet or commencing or discontinuing any course of treatment. Do not ignore or delay obtaining professional medical advice because of information accessed through ASN. Call 911 or your doctor for all medical emergencies.

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Tweet**:** Certain reflux and ulcer medications linked bone fractures in dialysis patients.
Twitter handle: @ChandanVangala

Facebook: Certain medications commonly used to treat heartburn, acid reflux, and ulcers are linked with higher bone fracture risks among patients on dialysis, according to a new study. Almost three-quarters of patients who had a hip fracture had used the medications in the 3 years preceding their event. The findings appear in the *Clinical Journal of the American Society of Nephrology*.

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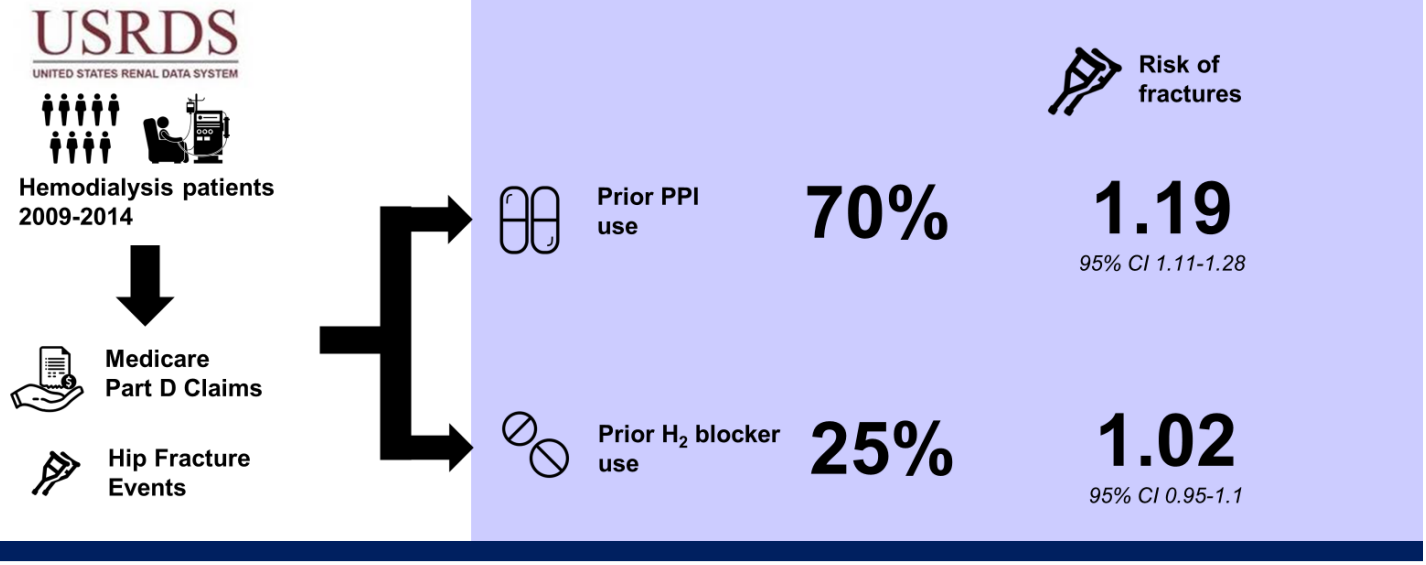
Visual Abstract created by CJASN Visual Abstract Editors and further edited by Chandan Vangala:

Do Proton Pump Inhibitors or Histamine-2 Receptor Antagonists increase the Risk of Hip Fracture Among Patients on Hemodialysis ?

CJASN
Clinical Journal of American Society of Nephrology



Conclusion: Among patients with end-stage kidney disease on hemodialysis, PPIs, and not histamine-2 receptor antagonists, were associated with hip fracture events.

Chandan Vangala, Jingbo Niu, Colin Lenihan, William Mitch, Sankar Navaneethan, and Wolfgang Winkelmayer. *Proton Pump Inhibitors, Histamine-2 Receptor Antagonists, and Hip Fracture Risk Among Patients on Hemodialysis.*
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