



GHAPP

Gastroenterology & Hepatology
Advanced Practice Providers

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Proton Pump Inhibitors: Point/Counterpoint

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Disclosures

Shana Arnhold, MPA, PA-C

Speakers Bureau: Takeda, Clinical Area- IBD

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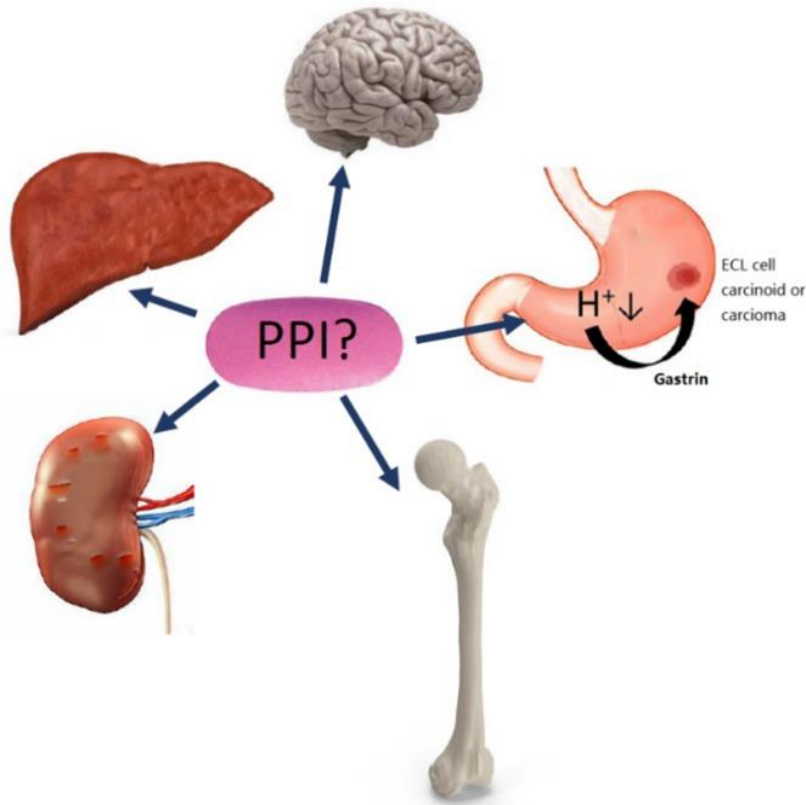
PPI Use

- PPIs are one of the most widely prescribed classes of medications in the world
- Proton pump inhibitors (PPIs) inhibit H-K-ATPase, the final step of gastric acid secretion by parietal cells
 - Indicated for GERD/Barrett's esophagus, PUD (peptic ulcer disease), NSAID/stress ulcer, H Pylori treatment, Zollinger-Ellison syndrome

How Do PPIs Work?

- Animated video – Dr Jehad Hammad
- <https://www.youtube.com/watch?v=Fz871WjMzdU>

Proposed PPI Risks



- Gastric neoplasia
- Kidney disease
- Bone fractures
- Impaired absorption of micronutrients
- Dementia
- Liver disease
- Infection/GI effects

Gastric Neoplasia

Point

Mechanistic studies suggest that hypoacidity and hypergastrinemia increase the risk of gastric cancer in the corpus/fundus and this was also supported by some epidemiological studies¹

Counterpoint

- Incidence is small
- More likely are benign lesions
→ fundic gland polyps, black spots, cobblestone-like lesions
- Untreated H Pylori/ulcers could also result in malignancy

Kidney Disease – AIN

Point

- PPIs are now considered to be among the most common causes of drug-induced AIN worldwide²
- Symptoms of n/v, malaise, maybe oliguria, maybe no symptoms
- Presents 10 weeks to nine months after starting treatment, risk is not dose dependent
- Some evidence that they also increase the risk of CKD (mechanism not well understood)

Counterpoint

- If patient has been on PPI long term and renal function is normal, they should not be at risk for AIN
- Unclear whether they may still be at risk for CKD

Bone Health/Fracture Risk

Point

- PPI-induced hypochlorhydria can augment osteoclastic activity, thereby decreasing bone density^{4,5}.

Counterpoint

- The absorption of water-soluble calcium salts or calcium in dairy products are NOT impacted by PPI-induced hypochlorhydria.
- Suggestion that gastric hypoacidity affects bone metabolism negatively, however, the recent data from a randomized trial³ suggest that PPIs do not increase fracture risk.

Impaired Absorption of Micronutrients

Point

- B12 deficiency – increased risk in observational studies⁶
- Many studies have suggested an increased risk and that hypomagnesemia develops in a proportion of PPI users⁷
- A large case-control study found PPI use to be associated with an increased risk of iron deficiency⁸

Counterpoint

- B12 deficiency not reproduced in other studies
- Hypomagnesemia is rare and it seems that mainly patients who already use a diuretic are at risk⁷
- The magnitude of reduced iron absorption is most likely small in most individuals and the clinical importance has been questioned¹

Dementia

Point

- Some studies have found a significant association between use of PPIs and incident dementia⁹

Counterpoint

- Increased risk of dementia has not been reproduced in other epidemiological studies^{10,11}

Liver Disease

Point

- PPIs appear to increase the risk and severity of HE in cirrhosis patients, thought to be due to SIBO¹²
- Some evidence for increased r/o SBP, liver cancer as well^{13,14}

Counterpoint

- Epidemiological evidence is limited for the influence of PPIs on the pathogenesis of liver diseases including cancer (but bacterial overgrowth and altered bacterial composition are indeed well-documented)¹

Infection/GI effects

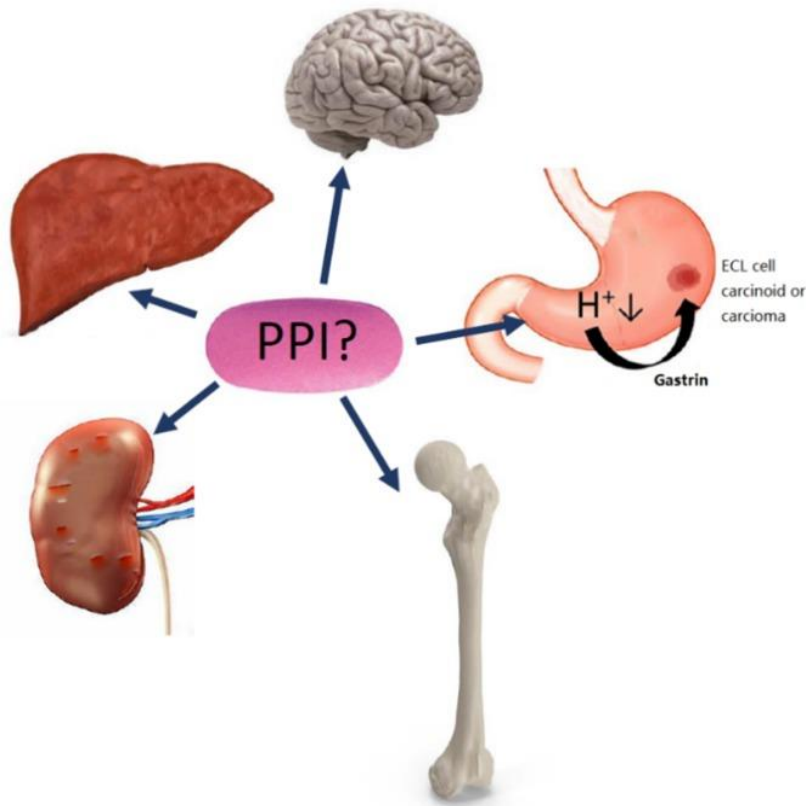
Point

- A 2017 meta-analysis of 50 observational studies found that PPI use was significantly associated with an increased risk of *C. difficile* infection (relative risk [RR] 1.3; 95% CI 1.1-14). The risk of *C. difficile* infection appears to be greater with PPIs as compared to H2 receptor antagonists¹⁵
- SIBO and altered bacterial composition also well-noted
- Increased risk of microscopic colitis, other enteric infections

Counterpoint

- Use of probiotics may decrease risk of diarrhea, SIBO – [Bacillus subtilis (B. subtilis) and Enterococcus faecium (E. faecium) 500mg TID]¹⁶

Proposed PPI Risks



- Gastric neoplasia
- Kidney disease*
- Bone fractures
- Impaired absorption of micronutrients*
- Dementia
- Liver disease
- Infection/GI effects*

Take-Home Points

- Many patients have appropriate indications for long-term PPI use that may outweigh the risks discussed.
- However, a large proportion of PPI users without indication have no benefits to outweigh any risk of side effects
- Some of the potential side effects may have an incubation time of years or even decades the risks and benefits of starting long-long PPI use should be carefully considered.

References

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