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Selecting the Right Patients for Proton Pump Inhibitor Discontinuation: A Teachable Moment

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Story from the Front Lines

A 72-year-old man presented to the emergency department with melena. His medical history included stroke and provoked deep venous thrombosis (DVT) eighteen years prior, and peptic ulcer disease (PUD) two years prior while using naproxen for chronic back pain. At that time, he was also taking warfarin and low-dose aspirin. Subsequently, his warfarin was replaced with aspirin 325 mg daily, which continues for stroke prevention. He still uses ibuprofen 200 mg three times weekly for back pain. Previous laminectomy, corticosteroid injections, and trials of tramadol, gabapentin, and acetaminophen were not effective. Two weeks ago, his primary care provider recommended stopping omeprazole because of potential adverse effects. In the emergency department, he was afebrile, pulse was 106 beats per minute, and blood pressure was 98/58. His hemoglobin was 13 mg/dl, down from 15 mg/dl recently; blood urea nitrogen was 47 mg/dl; serum creatinine was 1 mg/dl; and coagulation studies were normal. Upper endoscopy the following day revealed five non-bleeding ulcers in the gastric antrum not requiring endoscopic intervention. He was discharged one day later on omeprazole, to be continued indefinitely.

Teachable Moment

This patient had multiple risk factors for PUD, including advanced age, prior PUD, and use of aspirin and NSAIDs. In patients with pharmacologic risk factors, PPIs are remarkably effective at preventing bleeding PUD, reducing the odds by 79% in a meta-analysis of 18 randomized controlled trials.[1] Because older patients are at particularly high risk for developing PUD and complications such as bleeding, perforation, or death, they derive the

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most benefit from PPIs. Over five years, the number needed to treat to prevent one major upper GI bleed among aspirin users is 75 for patients aged 65–74 years, 23 for patients aged 75–84 years, and only 21 for patients aged 85 years or older.[2] An expert consensus statement from three professional societies supports the use of PPI gastroprotection in patients with multiple risk factors for bleeding PUD, including NSAIDs, anti-platelet therapy, anticoagulants, high-dose corticosteroids, prior PUD, untreated H. pylori infection, and age greater than 60–65 [3]. Nevertheless, PPIs are widely underused for this purpose.

Healthcare providers must carefully weigh the risks and benefits when prescribing, or deprescribing, PPIs, as with any therapy. For PPIs, this calculus has become more complicated because of recent concerns about adverse effects. Observational studies have demonstrated associations between PPIs and adverse effects in almost every organ system, including chronic kidney disease, bone fractures, clostridium difficile infection, and pneumonia. Considering these risks, many healthcare providers are inclined to discontinue PPIs when used for gastroprotection.[4] However, the clinical implications of these studies remain unclear.

First, significant questions remain about the extent to which residual confounding, a liability of observational designs, may explain many of the associations between PPIs and reported adverse effects: Patients who use PPIs tend to have worse health status than non-users, which may independently increase PPI users' risk of adverse effects. Second, the strength of association between PPIs and most of the hypothesized adverse effects are modest, around 0.1–0.5% absolute excess risk per patient/year. For example, one observational study found that in a 50-year-old man with normal kidney function, PPIs increase the relative risk for CKD by 10–20%, which is equivalent to an absolute excess risk of only 0.1–0.3% per year.[5] This small increase in absolute risk may raise important questions about the contribution of PPIs to CKD on a population level, but may be of lesser concern when prescribing PPIs to an individual patient.

No validated risk stratification or decision support tools exist to help clinicians weigh PPI risks versus benefits for gastroprotection, an area future research must address. Until then, healthcare providers must exercise their clinical judgment but should be especially cautious about stopping PPIs in patients with multiple PUD risk factors. Indeed, expert opinion still supports PPI use for patients at "high risk" for PUD.[6] Conversely, for patients without an indication for ongoing PPI use (e.g., uncomplicated gastroesophageal reflux disease or dyspepsia), healthcare providers should consider a trial off PPI. For patients with suspected GERD, four to eight weeks of a PPI is an appropriate initial course. Many patients on long-term PPIs may have no identifiable indication.

In conclusion, although PPIs are one of the most commonly prescribed, and often overused, medications, they are also frequently underused for the prevention of PUD in high-risk patients. Healthcare providers must be diligent to assess risk factors for bleeding PUD when considering PPI discontinuation. Healthcare providers should prescribe a PPI to patients with multiple risk factors, in addition to carefully considering whether modifiable risk factors, such as full dose aspirin or unnecessary NSAIDs, can be reduced or eliminated. On the other hand, healthcare providers should strongly consider stopping PPIs when no clear

indication exists. Both inappropriate overuse and underuse of PPIs carry their own risks of preventable harm.

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