The Distressing Overuse of Gastric Acid Inhibitors

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Gastric acid secretion by parietal cells is an energy consuming process that concentrates H⁺ one million-fold. The energy required is produced by abundant mitochondria. High gastric acidity in combination with the proteolytic enzyme, pepsin, and the lipolytic enzyme, lipase, plays a key role in killing ingested microorganisms including bacteria [1, 2], viruses [3], and prions [4]. This corrosive juice can, however, overwhelm mucosal defense mechanisms leading to erosion and ulceration.

Stress ulcers and less severe damage to the gastric mucosa may develop in critically ill patients. The damage, which occurs predominantly in the oxyntic mucosa, is thought to be caused by tissue hypoxia [5, 6]. Hypovolemic or hypotensive patients are at obvious risk of developing such ulcers, but severe illness also increases the risk of stress ulcers [7, 8], particularly in patients requiring mechanical ventilation. Experimental studies have suggested that antisecretory medications, e.g. proton pump inhibitors (PPIs) and histamine H₂-receptor antagonists (H₂RAs), reduce development of ulcers in the oxyntic mucosa by decreasing energy expenditure as well as raising intragastric pH [9, 10].

In this issue of *Digestive Diseases and Sciences*, Koczka et al. [11] report the overuse of stress ulcer prophylaxis in a large medical center. This adds to a large body of literature reporting the inappropriate overprescription of PPIs.

Although the use of gastric acid inhibitors may reduce the risk of stress ulcers, it is important to target the therapy to patients at significant risk since PPIs have recently been associated with numerous adverse events, including infections. Gastric hypoacidity leads to bacterial overgrowth in the stomach and small intestine, in particular, an increase in gram negative and anaerobic bacteria [12, 13]. PPIs also increase the risk for *Clostridium difficile* infection (CDI) [14] and may predispose cirrhotic patients for spontaneous bacterial peritonitis [15, 16]. PPIs may also be associated with increased risk for respiratory infections, although the data are less clear [17, 18]. Nevertheless, in patients disposed to develop stress ulcers (that is patients with hypovolemia and/or hypoxia), it seems justified to prescribe prophylaxis with PPIs since the benefits of preventing a significant bleed in these very sick patients outweigh potential risks [19]. Critically ill patients probably profit from PPI stress ulcer prophylaxis, whereas in less ill patients with a minute risk of development of stress ulcers, the side effects may represent a greater risk for the patients than a possible small reduction in the risk of stress ulcer bleeding. In the present issue Koczka et al. [11] compared the attitude to stress ulcer prophylaxis between attending physicians and residents in a medical center in New York, reporting that half of the attending physicians thought that stress ulcer prophylaxis was indicated outside critical care settings.

Perhaps even more problematic than short-term overuse of PPIs during the hospital stay is the fact that most of these patients are discharged on PPIs and thus probably remain on these drugs for prolonged periods without a proper indication [20, 21]. After patients are on PPIs for more than 3 months, stopping may be difficult due to rebound acid hypersecretion-induced dyspepsia [22, 23].

In conclusion, stress ulcer prophylaxis with PPIs is indicated in critically ill patients with hypovolemia and/or

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tissue hypoxia since these patients are predisposed to stress ulcer bleeding and PPIs are the most effective agents to prevent this complication. As PPIs have recently been associated with a plethora of adverse events, including increased infection rates, these medications should be given for specific indications and for the least time necessary.

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