A new perspective on stress ulcer prophylaxis

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Gastric acid suppression by use of either antacids or histamine H_2-receptor antagonist therapy is the mainstay of stress ulcer prophylaxis. Available evidence indicating an antimicrobial role for gastric acid calls for the reevaluation of gastric acid suppression. A pH of greater than 4.0 leads to bacterial overgrowth and colonization of the upper gastrointestinal tract which has been associated with nosocomial pneumonia, bacterial translocation from the gut, systemic sepsis, and multiple-organ failure. The availability of alternative therapy should discourage the routine use of acid-suppression therapy in the critically ill patient.

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Stress-related gastric mucosal ulceration is a well-recognized occurrence in critically ill patients. Therapy of stress ulceration is directed toward the prevention of hemorrhage. Although the great majority of bleeding is occult, overt upper gastrointestinal bleeding in critically ill patients has a high mortality. Gastric acid suppression by means of antacids or histamine H_2-receptor antagonists has greatly reduced the incidence of bleeding. In light of recent discoveries about the antimicrobial effects of gastric acid and the possible complications associated with acid suppression, the empiric use of antacids and histamine H_2-receptor antagonists is questionable.

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Role of acid

Despite the role of acid in the activation of pepsinogen to pepsin, achlorhydric patients show little change in the absorption of protein or other nutrients. The fact that acid is secreted in the fasting state suggests a nondigestive role for gastric acid.

Bacterial translocation

Bacteria thrive and colonize the upper gastrointestinal tract as stomach pH rises above 4.0.[1] Loss of this antimicrobial defense mechanism can be detrimental in several ways. For example, wound infections after gastric surgery are significantly increased with bacterial overgrowth,[2] loss of gastric acidity may predispose to *Clostridium difficile* colitis,[1] and mechanically ventilated patients are subject to a higher incidence of nosocomial pneumonia.[3,4] Furthermore, bacterial colonization of the upper gastrointestinal tract may promote the translocation of bacteria and endotoxins into the systemic circulation.[5] The repercussions of bacterial translocation include sepsis and multiple-system organ failure. The organisms predominantly associated with multiple-organ failure are commonly cultured from the upper gastrointestinal tract.[6]

The rationale for inhibiting bacterial growth in the stomach is supported by the practice of "selective decontamination" of the digestive tract. This protocol, which uses nonabsorbable oral antibiotics to suppress the growth of aerobic gram-negative organisms while not affecting anaerobic flora, has shown a greater than 50% reduction in sepsis in selected patients.[7]

Gastric acid is not the sole agent in the pathogenesis of stress ulceration. It has been known that mucosal ischemia is the primary etiologic event. In fact, patients with ongoing shock may progress to life-threatening hemorrhage from stress ulceration despite acid-suppression therapy. Stress ulceration therefore is a sign of hypoperfusion rather than a problem of acid secretion.

Prophylaxis

If prophylaxis is desired, agents that maintain the integrity of the mucosal surface, yet do not interfere with gastric activity, should be considered. The commercially available agent sucralfate has been shown to be as effective as histamine H_2-receptor antagonists and antacids in the prevention of stress ulcer hemorrhage.[8,9] In addition, this agent is not associated with many of the drug interactions found with H_2-receptor antagonists. Furthermore, it does not require dosage adjustments for hepatic or renal failure.

Antimicrobial defense mechanism

Gastric acid may provide an important antimicrobial defense mechanism to thwart the colonization of the upper gastrointestinal tract with gram-negative pathogens. This mechanism may be important in the prevention of nosocomial pneumonia, sepsis, and multiple-organ failure in critically ill patients. The potential risks associated with bacterial overgrowth and the availability of effective alternative therapy should discourage the routine use of acid-suppression therapy in the intensive care unit patient.

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