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Stress Ulcer Prophylaxis

Evidence Based Medicine Guideline

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SUMMARY
The incidence of clinically important gastrointestinal bleeding due to stress ulceration has declined with advances in the resuscitation and management of critically ill patients. Maintaining adequate systemic perfusion and initiating early enteral nutrition play a significant role in preventing stress ulceration. The efficacy of histamine-2 receptor antagonists (H_2RAs), antacids, and proton-pump inhibitors (PPI) in preventing stress ulceration remains

RECOMMENDATIONS

- **Level 1**
  - **None**
- **Level 2**
  - **Stress ulcer chemoprophylaxis is indicated in patients with high-risk factors for clinically important upper gastrointestinal bleeding (UGIB) including:**
    - **Coagulopathy (platelets <50,000, INR >1.5, or aPTT >2x control in the absence of full anticoagulation)**
    - **Shock (hypotension requiring vasopressors/inotropes or mechanical circulatory support)**
    - **Chronic liver disease (history of cirrhosis or cirrhotic complications – portal hypertension, hepatic encephalopathy, varices, or TIPS)**
    - **Neurocritical care conditions (i.e. severe traumatic brain injury, acute spinal cord injury, subarachnoid hemorrhage, intracerebral hemorrhage)**
    - **Significant burn injury (total body surface area ≥ 20%)**
  - **Discontinue therapy when high-risk factor(s) is/are no longer present**
  - **Enteral nutrition is recommended to reduce clinically important UGIB**
  - **H_2RAs are preferred over PPIs given cost and ease of administration**
    - **A PPI is an alternative to a H_2RA in situations where H_2RA cannot be used**
- **Level 3**
  - **In patients without high-risk factors, chemoprophylaxis may be considered in patients with any of the following low-risk factors:**
    - **Recent gastrointestinal bleed within the past 3 months**
      - **Two or more of the following antithrombotics: P2Y12 inhibitors, aspirin, therapeutic anticoagulation**
    - **Mechanically ventilated patients without full enteral nutrition**
  - **Consider discontinuation of chemoprophylaxis in patients with surgical airways no longer requiring positive pressure ventilation without the presence of a high-risk factor**
  - **There is insufficient evidence to support the use of chemoprophylaxis in patients on corticosteroids regardless of dose**
  - **PPIs or H_2RAs as home medications should be evaluated for indication and continued if the indication still warrants therapy (e.g. 2+ antithrombotics with chemoprophylaxis outpatient)**

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

controversial. Prophylaxis using these medications is associated with potential adverse effects and drug interactions as well as additional cost. Given the controversial efficacy of these agents, their use should be limited to patients with high-risk factors. In addition, these guidelines are not intended for patients that have an indication for treatment with acid suppressive therapy, such as duodenal ulcer disease, gastroesophageal disease, etc.

INTRODUCTION

Stress ulceration is a form of hemorrhagic gastritis that may occur following trauma or critical illness (1). Although not completely understood, the pathophysiology is likely multifactorial. Inadequate systemic perfusion resulting in poor mucosal blood flow, and reperfusion injury play an important role in the development of stress ulceration (1,2). Decreased gastric pH, increased mucosal permeability, and alterations in normal protective mechanisms may also be contributing factors (2,3). There has been a decrease in the incidence of clinically important bleeding due to stress ulceration (1). This can likely be attributed to improved resuscitation, earlier initiation of enteral feeding, the cessation of high-dose steroids for traumatic brain and spinal cord injury, and possibly the use of pharmacologic prophylaxis.

Medications used for stress ulcer prophylaxis (SUP) act by inhibiting gastric acid secretion, neutralizing gastric acid, or protecting the gastric mucosa. The efficacy of H_2RAs and antacids has been extensively studied. Both placebo-controlled trials and meta-analyses, however, have yielded conflicting results (2). Similarly, PPIs for stress ulcer prophylaxis have been evaluated in a limited number of published trials. Although these agents effectively maintain gastric pH ≥ 4, this endpoint has not been proven to improve clinical outcomes. Additionally, superiority over H_2RAs has not been demonstrated in a well-designed trial. Many investigators now question the value of pharmacologic prophylaxis, especially in the setting of improved resuscitation techniques and early enteral feeding. A randomized, controlled trial that compared a PPI, H_2RA, and sucralfate with placebo in 287 high-risk trauma/surgery patients demonstrated no difference in clinically significant upper GI bleeding with percentages of 1%, 3%, 4%, and 1%, respectively (4). Prophylactic medications are associated with potential adverse effects such as increased risk of *Clostridium difficile* infection and ventilator associated pneumonia, and drug interactions as well as additional cost.

LITERATURE REVIEW

Risk Factors for Stress Ulceration

In a prospective multicenter study of 2,252 patients, Cook et al. identified respiratory failure (mechanical ventilation for at least 48 hours) and coagulopathy (platelet count <50,000 mm^3, INR >1.5, or aPTT > 2 times control) as independent risk factors for clinically important bleeding (5). Of the 33 patients (1.5%) with clinically important bleeding, 23 (70%) were receiving stress ulcer prophylaxis. However, the use of prophylaxis was not controlled, and various regimens were administered with 72% of patients receiving H_2RAs and 0.3% receiving a PPI. Enteral nutrition was not addressed. Almost half of the patients were admitted for cardiovascular surgery (49%) with only a small number of trauma patients represented (28 head injuries and 18 multiple traumas).

Two meta-analyses published in 2015 and 2019 demonstrated a decrease in GIB risk among neurocritical care patients who received SUP compared to those who did not. The incidence of GIB decreased to 11% compared to 33% with no SUP in a meta-analysis that incorporated all types of neurological injuries including traumatic brain injuries, spontaneous intracerebral hemorrhage and tumors (6). The benefit of SUP in the neurocritical care population was independent of any other risk factors (7). The studies incorporated both H_2RA and PPI use for SUP.

The data to support SUP for prevention of GIB in patients on corticosteroids remains controversial. A meta-analysis published in 2014 found no correlation between dose of corticosteroids and risk of GIB. This study found a trend toward less clinically significant GIB in patients on SUP (RR 1.97, 0.92-4.21) compared to no SUP (RR 3.32, 0.14-78.25) but did not reach statistical significance (8). An older prospective, randomized, placebo-controlled trial in neurosurgical patients, all on dexamethasone 4 mg Q6H, found a significant decrease in overt GIB in patients concurrently treated with H_2RAs (18%) vs placebo (40%) (p=0.028) (9). These findings further corroborate the known GIB risk for neurocritical care patients.

A subsequent multivariate analysis by Cook et al. identified maximum serum creatinine as a risk factor (RR 1.16 [95% CI 1.02-1.32]) for clinically important upper gastrointestinal bleeding (3). All patients received either ranitidine or sucralfate. The use of enteral feeding was not randomized. Enteral nutrition (RR 0.3 [95%CI 0.13-0.67]) and ranitidine (RR 0.39 [95%CI 0.17-0.83]) were both protective against stress ulceration. The overall incidence of clinically important gastrointestinal bleeding was 2.8%. None of the 147 trauma patients had clinically important bleeding.

Although other risk factors have been identified, they have not been well studied. These include sepsis, intensive care unit (ICU) stay greater than one week, and presence of occult bleeding for at least six days (2,10). There is evidence that the incidence of stress ulceration is higher when more than one risk factor is present (11).

Patients suffering burn or neurologic injury have frequently been excluded from studies due to their presumed high-risk for the development of stress ulcers. Additional populations frequently excluded from clinical trials include patients with a history of upper gastrointestinal hemorrhage, peptic ulcer disease, or non-steroidal anti-inflammatory drug (NSAID) use. Whether these conditions translate into an increased risk of acute, stress-induced bleeding is therefore unknown (5).

In 2018, the Stress Ulcer Prophylaxis in the Intensive Care Unit (SUP-ICU) trial evaluated IV pantoprazole vs. placebo in adult ICU patients at risk for GI bleeding. About three-quarters of patients were receiving mechanical ventilation and vasopressor or inotrope support. Of note, enteral nutrition was given in 58% of patients on day one with up to 85% of patients by day five. (12). Three years after this trial was published, a post-hoc analysis of the SUP-ICU trial sought to identify potential predictors of clinically important UGIB and overt GIB. Severity of illness, use of vasopressors or inotropes, and use of RRT were associated with increased risk of both clinically important UGIB and overt GIB (13).

Granholm et al. published a meta-analysis in 2019 that included 8 studies (n=116,497) to assess potential predictors of clinically important UGIB (14). Acute kidney injury was associated with a statistically significant increase in clinically important UGIB with male gender associated with a small increase in the risk. When high risk of bias studies were excluded, leaving two studies to evaluate, coagulopathy, shock, and chronic liver disease were associated with a statistically significant increase in clinically important UGIB. The effect of mechanical ventilation was unclear.

The Society of Critical Care Medicine (SCCM) and American Society of Health-System Pharmacists (ASHP) updated their guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults in 2024. After excluding studies with high-risk of bias, they suggest coagulopathy, shock, and chronic liver disease should be considered high-risk factors for clinically important upper GIB. Furthermore, mechanical ventilation alone probably is not a risk factor that necessitates SUP; however, it should be noted that mechanical ventilation may be inherent in the definition of critical illness. Additionally, they recommend using SUP in neurocritical care patients given physiologic changes that may result in hypersecretion of gastric acid (15).

Medication Risk Factors and De-Escalation of PPI therapy

There is currently insufficient data to recommend the routine use of SUP for patients on NSAIDs. A 2025 Cochrane review found that PPIs could reduce the incidents of ulcers, however the certainty of the evidence for this outcome was very low (16). When evaluating patients that are on dual antiplatelet therapy (DAPT) or triple therapy (aspirin, a $P2Y_{12}$ inhibitor, and an oral anticoagulant), there can be consideration in using SUP. Dual antiplatelet therapy with aspirin and a $P2Y_{12}$ receptor inhibitor confers a 2- to 3-fold increased risk of upper GI bleeding compared with aspirin alone (17). Based on the evidence from COGENT (Clopidogrel and the Optimization of Gastrointestinal Events Trial), the European Society of Cardiology (ESC) recommends PPI for all patients on DAPT (Class I, Level of Evidence B) (18,19). The ACC/AHA takes a more selective approach: PPI is recommended for DAPT patients with prior GI bleeding (Class I) and considered reasonable for those with advanced age or concomitant warfarin, corticosteroid, or NSAID use (Class IIa), while routine PPI use in low-risk DAPT patients is not recommended (Class III, no benefit) (19,20). Patients on triple antithrombotic therapy represent the highest-risk group for GI bleeding. Both the ESC and ACC/AHA recommend PPI gastroprotection for all patients on triple therapy (16,19,21).

The 2024 SCCM and ASHP Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults recommend that patients without risk factors for developing clinically important stress-related UGIB, but on a SUP agent before ICU admission, have the indication evaluated. They list recent UGIB, hypersecretory states, erosive esophagitis, and eradication of *Helicobacter pylori* infections as indications for PPIs and therapy or prevention of anaphylaxis, angioedema, or urticaria as indications for H_2RAs. There is no clear definition of recent UGIB listed in the guidelines; however, PPIs are typically continued for 4-12 weeks depending on the cause of the UGIB (15).

In 2017, Farrell et al. developed an evidence-based guideline to help clinicians deprescribe PPIs (22). The authors recommend continuing longterm PPI therapy in ambulatory patients for prevention of nonsteroidal anti-inflammatory

drug–induced ulcers, severe esophagitis, Barrett esophagus, idiopathic chronic ulcer, refractory gastroesophageal reflux disease, pathologic hypersecretory conditions (e.g., Zollinger-Ellison syndrome), and certain patients with a history of gastrointestinal ulcer with bleeding. They recommend de-prescribing PPIs in patients with a history of Helicobacter pylori infection, peptic ulcer disease, heartburn, dyspepsia, or gastroesophageal reflux disease but no present indication for antisecretory treatment. Deprescribing can be done by reducing the dose, stopping and using on-demand, or step-down therapy to H_2RAs.

Stress Ulceration and Enteral Feeding

A meta-analysis published in 2010 included 17 randomized, controlled trials that enrolled a total of 1,836 patients (23). This meta-analysis distinguished between studies that used early, adequate enteral nutrition from those that did not to assess the efficacy of stress ulcer prophylaxis. Results of the analysis demonstrated a reduced risk of GI bleeding with use of a H_2RA only in the sub-group of patients that did not receive enteral nutrition. Stress ulcer prophylaxis did not decrease the risk for GI bleeding in the patients that were fed enterally. Although prophylaxis with H_2RAs had no effect on pneumonia and hospital mortality overall, there was an increase in the incidence of hospital-acquired pneumonia and hospital mortality in the subgroup of patients that received stress ulcer prophylaxis plus enteral feeds.

In 2016, prospectively gathered data from 200 patients admitted to a single academic surgical/trauma ICU was analyzed for the risk of bleeding and the efficacy of their practice of discontinuing pharmacologic stress ulcer prophylaxis in patients tolerating full enteral nutrition (24). They found an overall incidence of 0.5% of clinically significant GI bleeding, with the subset of traumatic brain injury patients at only 0.68%, drastically different than the previously reported rate of 1.5%. Combined with the findings of a small randomized controlled, double blind, exploratory study enrolling 102 critically ill, mechanically ventilated patients that revealed no benefit (or harm) to adding pantoprazole to enteral nutrition (25), full enteral nutrition is probably adequate prophylaxis for stress ulcer prophylaxis in most critically ill patients.

The updated SCCM/ASHP Guidelines suggest enteral nutrition be used when feasible, and patients who do not have one of the three high risk factors (shock, coagulopathy, or chronic liver disease) for upper GIB are suggested to continue with use of chemoprophylaxis for SUP regardless of enteral nutrition use. It is suggested to avoid chemoprophylaxis in patients who are enterally-fed with low risk factors as concurrent use of SUP with enteral nutrition may increase the risk of pneumonia (15).

Histamine H_2 Antagonist (H_2RAs) vs. Proton Pump Inhibitors (PPIs)

Phillips et al. performed a prospective, open-label trial evaluating the efficacy of omeprazole suspension for stress ulcer prophylaxis in 75 critically ill patients (26). Patients were considered for the study if they were admitted to the surgical or burn ICU with an intact stomach, a nasogastric tube, and an anticipated ICU length of stay > 48 hours. They also had to have a gastric pH < 4, be on mechanical ventilation, and have an additional risk factor for stress ulceration. Patients were excluded if they were receiving enteral feedings through the nasogastric tube. Omeprazole suspension was administered as 40 mg, followed by a second 40 mg dose 6 to 8 hours later, then 20 mg daily until there was no longer a need for stress ulcer prophylaxis. Ten patients received H_2RAs prior to omeprazole suspension. Of the 65 patients who received omeprazole suspension as their initial prophylaxis, none developed overt or clinically significant upper gastrointestinal bleeding. Omeprazole significantly increased the mean gastric pH within 4 hours of the start of therapy (3.5 to 7.1).

In a similar study, the efficacy of omeprazole suspension was evaluated in 66 patients with severe trauma (27). In addition to mechanical ventilation, patients were required to have at least one other risk factor for stress ulceration. Patients were excluded if they were receiving gastric feedings. Omeprazole was administered as described in the previous study. None of the patients developed overt or clinically significant upper gastrointestinal bleeding. Gastric pH monitoring revealed a statistically significant increase following initiation of omeprazole therapy (3 patients required an increased dose to achieve adequate pH control).

Levy et al. compared the efficacy of omeprazole versus ranitidine for prophylaxis against clinically important gastrointestinal hemorrhage in 67 patients admitted to an ICU who had at least one risk factor for stress ulceration (28). Patients were randomized to receive ranitidine (50 mg bolus followed by 150 mg daily by continuous infusion or intermittent administration) or omeprazole (40 mg daily orally or via nasogastric tube). Clinically important bleeding occurred in significantly more ranitidine patients compared to omeprazole patients (31% versus 6%; p=0.013). It should be noted that the ranitidine patients had significantly more risk factors for stress ulceration than the omeprazole patients did. The use of enteral nutrition was not addressed.

A meta-analysis was performed pooling 936 patients from seven randomized, controlled trials to compare the efficacy and safety of H_2RAs to PPIs for stress ulcer prophylaxis (29). There was no statistically significant difference found in the incidence of upper gastrointestinal bleeding between PPIs and H_2RAs. In addition, no significant difference was found in the safety outcomes of pneumonia and ICU mortality.

In 2016, a randomized, double blind exploratory study out of Australia with the acronym "POP-UP" (Pantoprazole Or Placebo for stress Ulcer Prophylaxis: randomized double-blind exploratory study) suggested that in 214 mechanically ventilated patients, pantoprazole did not decrease bleeding events, nor did it increase the risk of ventilator associated pneumonias or *Clostridium difficile* infections (30). A similar study in 2017 of 91 patients randomized to pantoprazole or placebo from 10 ICUs in Canada and Australia found no statistically significant differences, but trends towards decreased ventilator associated pneumonias and *Clostridium difficile* infections in the placebo group (31). These two studies, and multiple pending pilot studies, suggest that with current critical care practices and modern incidences of stress ulcerative bleeding, the traditional decision to routinely give acid suppression therapy to ICU patients should be carefully studied and reconsidered.

In 2018, the Stress Ulcer Prophylaxis in the Intensive Care Unit (SUP-ICU) trial evaluated IV pantoprazole vs. placebo in adult ICU patients at risk for GI bleeding across six European countries (n=3,298). This was a multicenter, parallel-group, blinded trial. Risk factors for GIB included shock, use of anticoagulants (excluding prophylaxis), renal replacement therapy, mechanical ventilation expected to last > 24 hours, coagulopathy, or history of liver disease. No difference in death at 90 days (31.1% PPI vs. 30.4% placebo, p=0.76) or clinically important GIB, pneumonia, myocardial infarction (MI), or *Clostridium difficile* infections was found (12).

In 2020, data from the Proton Pump Inhibitors vs. Histamine-2 Receptor Blockers for Ulcer Prophylaxis Treatment in the Intensive Care Unit (PEPTIC) cluster crossover randomized controlled trial was published in JAMA (32). The multi-country trial included 26,828 mechanically ventilated ICU patients that were randomized into the proton pump inhibitor arm (13,436 patients) or histamine-2 receptor blocker arm (13,392 patients). 33% of the patients were admitted to the ICU after elective surgery and 18% after emergency surgery. The primary outcome of the trial was in-hospital mortality, which resulted in 18% mortality in the proton pump inhibitor arm and 18% in the histamine-2 receptor blocker arm. Overall, the PEPTIC trial did not show a statistically significant difference in all-cause mortality within 90 days during the index hospitalization for patients requiring mechanical ventilation within 24 hours of ICU admission when PPIs were used as the default stress ulcer prophylaxis medication compared to histamine-2 receptor blockers. In regard to upper gastrointestinal bleeding, 172 of 13,436 patients (1.3%) in the PPI group and 239 of 13,392 patients (1.8%) in the histamine-2 receptor blocker group had clinically important bleeds (p=0.009), however it is believed this may have been due to the number of patients in the trial taking PPIs prior to ICU admission with resultant rebound acid secretion for those who were switched to histamine-2 receptor blockers. There was no statistically significant difference in *Clostridium difficile* infections or ICU and hospital length of stay.

A meta-analysis published in 2019 sought to assess the effects of PPI or H_2RA with placebo or no prophylaxis. It included 41 randomized controlled trials with a total of 6,790 participants, although only three studies had a low risk of bias. They did not find an effect of SUP on mortality; however, the meta-analysis of the three low risk of bias trials did show a reduction in GIB with SUP versus placebo/no prophylaxis. The full meta-analysis showed a reduction in clinically important GIB with SUP, but this result was not confirmed by the trial sequential analysis. The effects of SUP on pneumonia, MI, and *Clostridium difficile* infections were inconclusive (33). In the following year, an updated meta-analysis that also included sucralfate was published that evaluated 74 randomized controlled trials with 39,569 patients. Results showed that both PPIs and H_2RAs probably reduce clinically important UGIB in patients at high risk for bleeding and PPIs may be more effective, but both of these agents probably have little or no impact on mortality although the possibility that PPIs may slightly increase mortality can't be excluded (34). Then, Boyd, et al. published a retrospective, single-center study with 3,873 ICU patients who received PPI or H_2RA for SUP within 24 hours of intubation. No difference in overall occurrence of GIB was shown between the two groups although 7 patients in the PPI group experienced a clinically significant GIB while no patients in the H_2RA group did (p=0.013). In-hospital mortality was also more likely to occur in the PPI group (42.1% vs. 29.1%, p<0.0001), although the PPI group had a higher severity of illness and more shock, coagulopathy, steroid use, and acute neuro conditions present (35).

Guidelines from SCCM and ASHP regarding SUP in critically ill patients were updated in 2024, which suggested using either PPIs or H_2RAs as first-line agents for chemoprophylaxis when high-risk factors are present. This recommendation was made given the uncertainty of evidence regarding outcomes of mortality with PPIs but did

note that PPIs were associated with reduced clinically important upper GIB compared with H_2RAs despite the mixed results of increased mortality with their use. These medications should be used at low doses, which the guidelines defined as ≤ 40 mg daily of pantoprazole/omeprazole/esomeprazole or ≤ 40 mg daily of famotidine (15).

After the updated guidelines were published in 2024, the Reevaluating the Inhibition of Stress Erosions (REVISE) trail was published. This was a large multicenter, blinded randomized controlled trial across 8 countries, including the US and Canada, evaluated pantoprazole 40 mg IV daily (n=2,417) compared to placebo (n=2,404) in mechanically ventilated adult ICU patients. About 70% of patients in both groups were on vasopressors or inotropes, less than 10% on RRT, 35% on steroids, and 23% on pre-hospital acid suppression with the majority being on a PPI. There was significantly less clinically important UGIB in the PPI group (1% vs. 3.5%). The primary safety outcome of death from any cause at 90 days showed no significant difference between groups (36). Later that year, an updated meta-analysis was published with 12 trials (9,533 patients), of which included the REVISE trial (2024) and SUP-ICU (2018) trial, to evaluate the safety and efficacy of PPIs for SUP compared to placebo or no SUP. PPIs were associated with a reduced incidence of clinically important upper GIB with no effect on pneumonia and little to no effect on *Clostridium difficile* infection. The effect on mortality differed - mortality may be decreased in less severely ill patients and may be increased in more severely ill patients (37).

In contrast to the SCCM/ASHP 2024 Guidelines, the 2026 Surviving Sepsis Guidelines suggests using SUP with PPIs over not using chemoprophylaxis for stress ulcers; however, the PICO question was only focused on PPIs because recent trials examining SUP used PPIs and prior network meta-analysis suggested PPIs may be superior to H_2RAs in preventing clinically important upper GIB, although the effect on mortality remains unclear. They further state H_2RAs are a reasonable alternative in the absence of PPIs (38).

Sucralfate

Sucralfate is a molecular complex of sucrose, sulfate, and aluminum that is thought to form a protective barrier on the mucosal surface of the stomach, decreasing acid's erosive effect. It has been historically used as an adjunct to PPI and H_2RA in refractory ulcerative GI bleeding or in patients intolerant to these medications.

In 2016, Gindlinger et al. performed a retrospective study after perceiving an association between ventilator acquired pneumonia and ventilator bundle compliance (39). Their bundle elements included stress ulcer prophylaxis, head of bed elevation to 30º, daily sedation vacation, and deep-venous thrombosis prophylaxis, similar to the 2005 study by Rezar that saw ventilator acquired pneumonias decrease by 45% (40). They retrospectively reviewed 504 patients and evaluated those receiving sucralfate as stress ulcer prophylaxis versus pantoprazole, omeprazole, or famotidine. In the PPI/H_2RA group, they found 10.2 ventilator associated pneumonias per 1,000 ventilator days versus 3.7 ventilator associated pneumonias per 1,000 ventilator days in the sucralfate group. Furthermore, the type of pneumonia contracted was significantly different, with the sucralfate group incurring oropharyngeal flora bacteria compared with gram negative rods, methicillin resistant Staphylococcus aureus and Pseudomonas in the PPI/H_2RA group. These initial data suggest a promising role for sucralfate as stress ulcer prophylaxis in at risk patients.

Four years later, Wang et al. published an updated meta-analysis that also included the newly published PEPTIC trial. Sucralfate showed no important effects on clinically important UGIB when compared to placebo. In comparison to PPIs, the PPIs showed a probable reduction in clinically important UGIB, and the comparison to H_2RAs suggested a reduction in clinically important UGIB with H_2RAs over sucralfate (34).

There is no recommendation for or against the use of sucralfate in the 2024 SCCM/ASHP Guidelines; however, they do note it was associated with less pneumonia compared with PPIs or H_2RAs but these studies targeted gastric pH values > 3.5, which could predispose patients to pneumonia via alteration of bacterial flora. Ultimately, PPIs or H_2RAs are recommended for chemoprophylaxis (15).

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