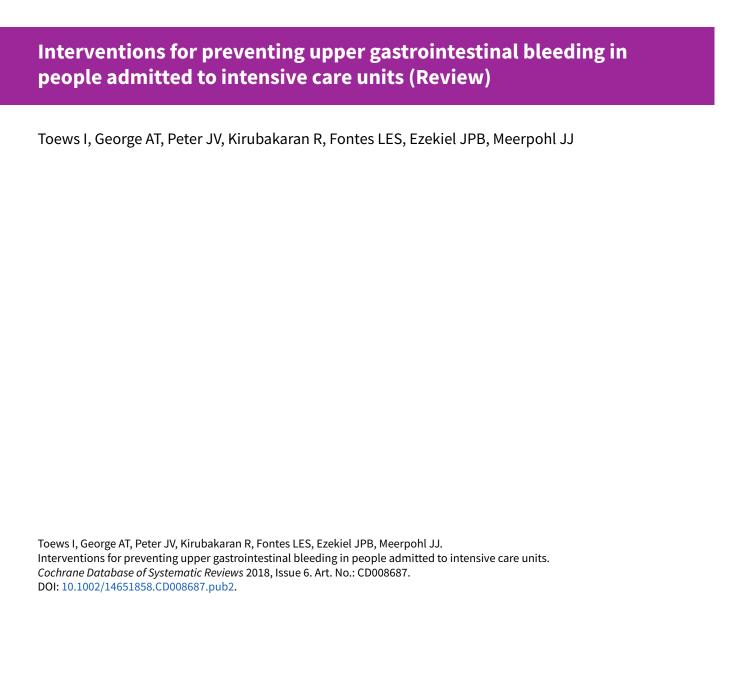


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[Intervention Review]

Interventions for preventing upper gastrointestinal bleeding in people admitted to intensive care units

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ABSTRACT

Background

Upper gastrointestinal (GI) bleeding due to stress ulcers contributes to increased morbidity and mortality in people admitted to intensive care units (ICUs). Stress ulceration refers to GI mucosal injury related to the stress of being critically ill. ICU patients with major bleeding as a result of stress ulceration might have mortality rates approaching 48.5% to 65%. However, the incidence of stress-induced GI bleeding in ICUs has decreased, and not all critically ill patients need prophylaxis. Stress ulcer prophylaxis can result in adverse events such as ventilator-associated pneumonia; therefore, it is necessary to evaluate strategies that safely decrease the incidence of GI bleeding.

Objectives

To assess the effect and risk-benefit profile of interventions for preventing upper GI bleeding in people admitted to ICUs.

Search methods

We searched the following databases up to 23 August 2017, using relevant search terms: MEDLINE; Embase; the Cochrane Central Register of Controlled Trials; Latin American Caribbean Health Sciences Literature; and the Cochrane Upper Gastrointestinal and Pancreatic Disease Group Specialised Register, as published in the Cochrane Library (2017, Issue 8). We searched the reference lists of all included studies and those from relevant systematic reviews and meta-analyses to identify additional studies. We also searched the World Health Organization International Clinical Trials Registry Platform search portal and contacted individual researchers working in this field, as well as organisations and pharmaceutical companies, to identify unpublished and ongoing studies.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-RCTs with participants of any age and gender admitted to ICUs for longer than 48 hours. We excluded studies in which participants were admitted to ICUs primarily for the management of GI bleeding and studies that compared different doses, routes, and regimens of one drug in the same class because we were not interested in intraclass effects of drugs.

Data collection and analysis

We used standard methodological procedures as recommended by Cochrane.



Main results

We identified 2292 unique records. We included 129 records reporting on 121 studies, including 12 ongoing studies and two studies awaiting classification.

We judged the overall risk of bias of two studies as low. Selection bias was the most relevant risk of bias domain across the included studies, with 78 studies not clearly reporting the method used for random sequence generation. Reporting bias was the domain with least risk of bias, with 12 studies not reporting all outcomes that researchers intended to investigate.

Any intervention versus placebo or no prophylaxis

In comparison with placebo, any intervention seems to have a beneficial effect on the occurrence of upper GI bleeding (risk ratio (RR) 0.47, 95% confidence interval (CI) 0.39 to 0.57; moderate certainty of evidence). The use of any intervention reduced the risk of upper GI bleeding by 10% (95% CI -12.0% to -7%). The effect estimate of any intervention versus placebo or no prophylaxis with respect to the occurrence of nosocomial pneumonia, all-cause mortality in the ICU, duration of ICU stay, duration of intubation (all with low certainty of evidence), the number of participants requiring blood transfusions (moderate certainty of evidence), and the units of blood transfused was consistent with benefits and harms. None of the included studies explicitly reported on serious adverse events.

Individual interventions versus placebo or no prophylaxis

In comparison with placebo or no prophylaxis, antacids, H2 receptor antagonists, and sucralfate were effective in preventing upper GI bleeding in ICU patients. Researchers found that with H2 receptor antagonists compared with placebo or no prophylaxis, 11% less developed upper GI bleeding (95% CI -0.16 to -0.06; RR 0.50, 95% CI 0.36 to 0.70; 24 studies; 2149 participants; moderate certainty of evidence). Of ICU patients taking antacids versus placebo or no prophylaxis, 9% less developed upper GI bleeding (95% CI -0.17 to -0.00; RR 0.49, 95% CI 0.25 to 0.99; eight studies; 774 participants; low certainty of evidence). Among ICU patients taking sucralfate versus placebo or no prophylaxis, 5% less had upper GI bleeding (95% CI -0.10 to -0.01; RR 0.53, 95% CI 0.32 to 0.88; seven studies; 598 participants; moderate certainty of evidence). The remaining interventions including proton pump inhibitors did not show a significant effect in preventing upper GI bleeding in ICU patients when compared with placebo or no prophylaxis.

Regarding the occurrence of nosocomial pneumonia, the effects of H2 receptor antagonists (RR 1.12, 95% CI 0.85 to 1.48; eight studies; 945 participants; low certainty of evidence) and of sucralfate (RR 1.33, 95% CI 0.86 to 2.04; four studies; 450 participants; low certainty of evidence) were consistent with benefits and harms when compared with placebo or no prophylaxis. None of the studies comparing antacids versus placebo or no prophylaxis provided data regarding nosocomial pneumonia.

H2 receptor antagonists versus proton pump inhibitors

H2 receptor antagonists and proton pump inhibitors are most commonly used in practice to prevent upper GI bleeding in ICU patients. Proton pump inhibitors significantly more often prevented upper GI bleeding in ICU patients compared with H2 receptor antagonists (RR 2.90, 95% CI 1.83 to 4.58; 18 studies; 1636 participants; low certainty of evidence). When taking H2 receptor antagonists, 4.8% more patients might experience upper GI bleeding (95% CI 2.1% to 9%). Nosocomial pneumonia occurred in similar proportions of participants taking H2 receptor antagonists and participants taking proton pump inhibitors (RR 1.02, 95% CI 0.77 to 1.35; 10 studies; 1256 participants; low certainty of evidence).

Authors' conclusions

This review shows that antacids, sucralfate, and H2 receptor antagonists might be more effective in preventing upper GI bleeding in ICU patients compared with placebo or no prophylaxis. The effect estimates of any treatment versus no prophylaxis on nosocomial pneumonia were consistent with benefits and harms. Evidence of low certainty suggests that proton pump inhibitors might be more effective than H2 receptor antagonists. Therefore, patient-relevant benefits and especially harms of H2 receptor antagonists compared with proton pump inhibitors need to be assessed by larger, high-quality RCTs to confirm the results of previously conducted, smaller, and older studies.

PLAIN LANGUAGE SUMMARY

Interventions for preventing upper gastrointestinal bleeding in people on intensive care units

Review question

We reviewed the evidence about benefits and harms of interventions to prevent clinically important upper gastrointestinal (GI) bleeding in patients who were admitted to the intensive care unit (ICU).

Background

Stress ulcers are seen as superficial damage in the mucous lining of the stomach or intestines that can occur as the result of shock, sepsis, or trauma. Depending on the severity of the damage, afflicted areas may become sore and may start to bleed to varying degrees. Upper GI bleeding due to stress ulcers is a major contributor to increased severity of illness and death among people admitted to ICUs. However,



standards of care have improved, and the incidence of upper GI bleeding in ICUs has decreased. Thus, not all critically ill patients need preventive treatment.

Stress ulcer prophylaxis can result in negative effects such as ventilator-associated pneumonia (VAP). VAP is a lung infection caused by bacteria in people who are being mechanically ventilated. VAP usually manifests as fever, cough, and purulent sputum. The risk for VAP is increased in patients with severe illness, increased length of hospital stay, or use of stress ulcer prophylaxis. Hence, it is necessary to evaluate strategies that safely decrease the incidence of upper GI bleeding.

Study characteristics

The evidence is current to August 2017. We included 106 studies with a total of 15,027 critically ill participants of any age and any gender.

Key results

Relevant effects were found for the following drugs: H2 receptor antagonists, antacids, sucralfate, and proton pump inhibitors.

H2 receptor antagonists inhibit gastric acid secretion by blocking histamine receptors but can cause a small number of blood platelets (thrombocytopaenia), inflammation of the kidney (interstitial nephritis), and confusion. Antacids neutralise stomach acid but may cause diarrhoea or constipation. Proton pump inhibitors inhibit the final stage of gastric acid production, and it has been found that they may be associated with increased risk of *Clostridium difficile* diarrhoea. Ulcer protective agents, such as sucralfate, create a barrier between the gastric acid and the gastric mucosa by coating it. They may, however, cause constipation and interfere with the absorption of certain antibacterial agents.

In comparison with placebo or no preventive treatment, H2 receptor antagonists, and sucralfate might be effective in preventing clinically important upper GI bleeding in ICU patients. Hospital-acquired pneumonia was most likely to occur in ICU patients taking either H2 receptor antagonists or sucralfate when compared with patients given placebo or no preventive treatment.

Evidence of low certainty suggests that proton pump inhibitors were more effective than H2 receptor antagonists in preventing upper GI bleeding in ICU patients. With proton pump inhibitors, 25 of 1000 people were likely to develop upper GI bleeding, and with H2 receptor antagonists, 73 of 1000 people (95% confidence interval 46 to 115 people) were likely to develop upper GI bleeding. The effect of H2 receptor antagonists versus proton pump inhibitors with respect to the risk for developing hospital-acquired pneumonia was consistent with benefits and harms.

Quality of the evidence

Our certainty in the evidence ranged from low to moderate. For effects of different interventions compared with placebo or no prophylaxis, the certainty of evidence was moderate (H2 receptor antagonists) or low (antacids and sucralfate). For effects of H2 receptor antagonists compared with placebo or no preventive treatment on risk of hospital-acquired pneumonia, the certainty of evidence was low. For effects of H2 receptor antagonists compared with proton pump inhibitors on hospital-acquired pneumonia, the certainty of evidence was also low.