Stress ulcer prophylaxis: friend or foe?

Stress ulcers are gastric mucosal defects that occur as a result of the physiological stress associated with serious illness. They may result in overt gastrointestinal bleeding in up to 8.5% of patients admitted to the intensive care unit. Numerous risk factors for stress ulceration have been identified including shock, sepsis, burns, head injury, renal failure, hepatic failure, acute respiratory distress syndrome, coagulopathy, mechanical ventilation and steroid therapy.

Many intensive care units incorporate stress ulcer prophylaxis as a component of the ventilator care bundle. The main pharmacological methods used are histamine-2 receptor antagonists and proton pump inhibitors. This article reviews the case for and against their use based on current evidence.

The case for

Cook et al (1996), in a systematic review of randomized trials, demonstrated that those randomized to receive histamine-2 receptor antagonists had a lower incidence of clinically significant bleeding in comparison to placebo or control. This prompted the routine use of histamine-2 receptor antagonists for stress ulcer prophylaxis in many units. Increasingly proton pump inhibitors have been used as first-line agents as they are better able to raise gastric pH and their effect is more sustained in comparison to histamine-2 receptor antagonists, thus they are perceived to be more efficacious at reducing bleeding from stress ulcers. However, Lin et al (2010) found no difference in efficacy between histamine-2 receptor antagonists and proton pump inhibitors in reducing bleeding.

Stress ulcer prophylaxis agents are cheap and convenient to administer. If they reduce the incidence of gastrointestinal bleeds, which are associated with a prolonged intensive care unit stay, then they may confer an economic benefit. Significant bleeding may also be associated with transfusion, gastrointestinal instrumentation and withdrawal of venous thromboembolism prophylaxis. Prevention of bleeding from stress ulcers is generally an easier route than cure.

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The case against

Alterations in upper gastrointestinal bacterial flora are known to occur with therapies that affect gastric pH. Micro-aspiration of these bacteria may lead to development of pneumonia. In a meta-analysis Messori et al (2000) questioned the efficacy of ranitidine, stating it was no more effective than placebo and may increase the risk of nosocomial pneumonia. Lin et al (2010) found no difference between histamine-2 receptor antagonists and proton pump inhibitors in the risk of developing nosocomial pneumonia.

Early enteral feeding is frequently undertaken in intensive care unit patients, in stark contrast to the early trials and meta-analyses demonstrating a benefit of stress ulcer prophylaxis when patients were often kept nil by mouth. Marik et al (2010) found that in those patients who were fed enterally, histamine-2 receptor antagonists did not reduce the risk of enteral bleeding. They also found that, in those patients being fed enterally, stress ulcer prophylaxis increased the risk of nosocomial pneumonia.

No study has been able to demonstrate a statistically significant reduction in mortality with the use of stress ulcer prophylaxis among intensive care unit patients. Interestingly Marik et al (2010) found that use of histamine-2 receptor antagonists in patients who were being enterally fed increased the risk of mortality.

Gastric acid is an important innate protective process against the ingestion of pathogenic organisms. Cunningham et al (2003) found the use of proton pump inhibitors to be associated with an increased risk of *Clostridium difficile* infection. Colitis resulting from infection is associated with significant morbidity and mortality.

Conclusions

The evidence for the use of histamine-2 receptor antagonists and proton pump inhibitors for stress ulcer prophylaxis is controversial. Proton pump inhibitors do not appear to confer any added benefit beyond that of histamine-2 receptor antagonists. The use of stress ulcer prophylaxis has not been associated with a reduction in mortality, although it may be associated with reduced morbidity, particularly in those at a high risk of gastrointestinal bleeding. However, this must be balanced with the possible increased risk of ventilator-associated pneumonias and *C. difficile* infection. Stress ulcer prophylaxis should only be used in those with a high risk of gastrointestinal bleeding and its requirement should be reviewed on a daily basis.

The efficacy of enteral feeding itself in reducing bleeding is unknown, this is particularly pertinent as early enteral feeding is frequently now undertaken. A large multi-centred prospective randomized controlled trial is required to elucidate the efficacy of enteral feeding *vs* stress ulcer prophylaxis on mortality and morbidity in intensive care unit patients to move this debate forward. **BJHM**

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