

Meta-analysis: Prophylaxis with anti-ulcer therapy reduces clinically important GI bleeding in critically ill patients

Cook DJ, Reeve BK, Guyatt GH, et al. *Stress ulcer prophylaxis in critically ill patients. Resolving discordant meta-analyses.* JAMA. 1996 Jan 24/31;275:308-14.

Objective

To resolve the discrepancies in previous systematic reviews and to evaluate the effectiveness of stress ulcer prophylaxis in critically ill patients.

Data sources

Studies were identified by searching MEDLINE and EMBASE using the keywords gastrointestinal hemorrhage, critical care, and clinical trials. Reference lists of identified articles were scanned, personal and pharmaceutical files were searched, conference reports were scanned, SCISEARCH was searched, and experts were contacted to identify additional studies. Articles available as of 1 January 1995 were included.

Study selection

Studies were selected if they were randomized controlled trials that compared prophylactic drugs with each other or with no therapy in critically ill patients and if the outcomes were gastrointestinal (GI) bleeding or pneumonia. Methodologic quality was assessed in duplicate.

Commentary

For the clinician, meta-analyses are especially helpful in areas of controversy where many studies have been published without yielding a clear result. One such area is the evaluation of agents for stress ulcer prophylaxis and the accompanying incidence of nosocomial pneumonia. Many of the individual studies are too small to prevent false-negative results (β -error). In the report by Cook and colleagues, the meta-analysis was taken a step further by comparing 2 previous meta-analyses on this subject. The authors clearly describe their rigorous efforts to locate and evaluate all randomized controlled trials. Their meta-analysis was made more clinically relevant by comparing only the most commonly used agents: antacids, H₂RAs, and sucralfate.

Data extraction

Data were extracted on patient characteristics, intervention, and outcomes. Overt bleeding was defined as hematemesis, bloody gastric aspirate, melena, or hematochezia. Clinically important bleeding was defined as overt bleeding associated with hemodynamic changes or the need for transfusion. Data were extracted independently in duplicate. The authors of included studies were asked to check the extracted data for accuracy.

Main results

The sources of discrepancies among 2 previous meta-analyses and the current one included slight differences in the question, incomplete identification of relevant studies, differential inclusion of non-English-language and nonrandomized trials, different definitions of bleeding, and different statistical methods. Of 269 retrieved studies, 63 met the selection criteria. Prophylaxis with either histamine₂-receptor antagonists (H₂RAs) or sucralfate reduced the incidence of overt GI bleeding when compared with placebo or no therapy (common odds ratio [OR] 0.58, 95% CI 0.42 to 0.79; OR 0.58, CI 0.34 to 0.99, respectively). H₂RAs were also superior to antacid therapy (OR 0.56, CI

0.37 to 0.84). H₂RAs decreased the incidence of clinically important bleeding when compared with no therapy (OR 0.44, CI 0.22 to 0.88). Insufficient data were available to evaluate the effect of sucralfate on clinically important bleeding. A trend exists toward an increased risk for pneumonia with H₂RAs when compared with no prophylaxis (OR 1.25, CI 0.78 to 2.00). Sucralfate was associated with a strong but nonsignificant trend toward a lower incidence of nosocomial pneumonia when compared with antacids (OR 0.80, CI 0.56 to 1.15) and H₂RAs (OR 0.78, CI 0.60 to 1.01) and with decreased mortality (OR 0.83, CI 0.62 to 1.09) when compared with H₂RAs.

Conclusion

Prophylaxis with anti-ulcer regimens reduces overt and clinically important gastrointestinal bleeding in critically ill patients.

Source of funding: Not stated.

For article reprint: Dr. D.J. Cook, Department of Medicine, Fontbonne Building, St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, Ontario L8N 4A6, Canada. FAX 905-521-6068.

Abstract and Commentary also published in *ACP Journal Club*. 1996;125:9.

Although this meta-analysis will not end the clinical controversy, some valuable information is provided. First, no apparent difference exists in efficacy among the 3 agents for the prevention of stress ulcers. Given equal efficacy, the trend in favor of lower incidence of nosocomial pneumonia for sucralfate, plus the trend for H₂RAs to be associated with a higher incidence of nosocomial pneumonia when compared with no prophylaxis, lends considerable strength to the argument for making sucralfate the treatment of choice for prophylaxis of stress ulceration in critically ill patients.

Many of the trials in this meta-analysis were completed in the 1970s and 1980s. Currently, as reported by Cook and by others (1, 2), most critically ill patients appear to be at low risk

for clinically important GI bleeding. High-risk patients are identified as those who need mechanical ventilation for 48 hours or those with coagulopathy (1). Additional research with economic analysis should compare strategies of universal anti-ulcer prophylaxis with high-risk-only prophylaxis and no prophylaxis.

Mitchell Levy, MD
Saint Anne's Hospital
Fall River, Massachusetts, USA

References

1. Cook DJ, Fuller H, Guyatt GH, et al, for the Canadian Critical Care Trials Group. *N Engl J Med*. 1994;330:377-81.
2. Zandstra DE, Stoutenbeck CP. *Intensive Care Med*. 1994;20:335-40.