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**Reference:** Selvanderan SP, Summers MJ, Finnis ME, et al. Pantoprazole or Placebo for Stress Ulcer Prophylaxis (POP-UP): Randomized Double-Blind Exploratory Study. *Crit Care Med* 2016;44:1842–185

**PICO Question:** Is prophylactic administration of a PPI overtly harmful or beneficial in invasively mechanically ventilated patients?

**Introduction:** Clinically significant GI bleeding is associated with increased mortality and longer ICU stays, but has been decreasing over time. This may reflect changes in practice including earlier initiation of enteral feeding. There have been few studies comparing proton pump inhibitors with placebo in prevention of GI bleeding in critically ill. Recent studies of PPIs have shown association with ventilator-associated pneumonia and *Clostridium difficile* along with adverse cardiac events. Current practice and recommendations in preventing GI bleeding in critically ill patients do not have a large amount of supporting evidence.

**Methods:** A prospective randomized double-blind parallel-group study of university affiliated medical-surgical ICU mechanically ventilated patients suitable for enteral nutrition. 214 participants were randomly assigned to receive 40 mg of pantoprazole IV or placebo once daily. The intervention was given once daily until the patient was no longer intubated or a maximum of 14 days.

**Results:** Major outcomes measured were significant GI bleeding, infective ventilator associated complication/pneumonia, and *Clostridium difficile* infection. The study found no statistically significant evidence of benefit or harm with the prophylactic administration of a PPI in ventilated patients expected to receive enteral nutrition. There were no episodes significant bleeding, three patients with ventilator associated complications and one patient with *C. difficile*. There was no difference between the interventions in mortality at 90 days.

**Discussion:** Although relatively small, the data suggests uncertainty as to the benefits and harm associated with use of PPIs. The study looked at a patient population considered to be at the greatest risk for stress ulcers and GI bleeding, critically ill ventilated patients. Given the lack of definitive benefit or harm, this article should cause second thought in those empirically ordering PPIs in all intubated patients regardless of feeding plans.

**Limitations:** The small study size and limited number of patients with complications limit the study. The small sample and infrequency of complications may have been underpowered to detect potential harmful events of PPIs. The study also only included patients expected to start feeding within 48 hours of admission, so it may not be generalizable to ICUs that have longer fasting periods.

**Bottom Line:** Given the recent concerns over PPIs association with adverse events, more investigation is necessary regarding the practice of prophylactic use in intubated patients.

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