Cost-effectiveness analysis of high-dose omeprazole infusion before endoscopy for patients with upper-GI bleeding

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Background: The use of intravenous (IV) proton pump inhibitors (PPI) before an endoscopy in upper-GI bleeding (UGIB) was shown to reduce the need of endoscopic therapy and shorten hospital stay.

Objective: To investigate whether preemptive use of a PPI in UGIB is a cost-effective strategy.

Design: A decision analysis model that represents treatment pathways for patients with UGIB was constructed and structuralized by 30-day outcomes. Direct costs of medical treatment, diagnostic and therapeutic endoscopy, endoscopic re-treatment, surgery, and hospitalization were analyzed.

Setting: Prince of Wales Hospital, Hong Kong.

Patients: A total of 631 patients were recruited. Sixty patients (19.1%) in the PPI group and 90 patients (28.4%) in the placebo group required endoscopic hemostasis at index endoscopy.

Main Outcome Measurements: The primary measurements were cost-effectiveness ratios and incremental cost-effectiveness ratios (ICER) to avert endoscopic therapy between PPI and placebo treatment. Sensitivity analyses were conducted by varying the cost of endoscopy, hospitalization, the incidence rate of endoscopic therapy, and the proportion of bleeding peptic ulcers.

Results: The overall direct cost per patient was U.S. dollars (USD) $2813 for PPI treatment and USD $2948 for the placebo. A PPI reduced endoscopic therapy by 7.4% and resulted in a lower cost-effectiveness ratio per endoscopic therapy averted (USD $3561) than the placebo (USD $4117). The ICER value was USD –$1843, which indicated that preemptive PPI treatment is more effective and less costly for UGIB. When the proportions of patients with peptic ulcer bleeding were greater than 8.3%, the preemptive PPI treatment remained cost saving.

Conclusions: Preemptive use of IV PPI before an endoscopy is a cost-effective strategy in the management of UGIB. (Gastrointest Endosc 2008;67:1056-63.)

Upper-GI bleeding (UGIB) is a life-threatening disease, with mortality rates ranging from 5% to 15%.[1] Endoscopic therapy has been proven to be effective in controlling active bleeding.[2,3] Randomized controlled trials showed that high-dose intravenous (IV) infusion of proton pump inhibitors (PPI) after endoscopic hemostasis reduced the rate of recurrent bleeding in patients with a bleeding peptic ulcer compared with a placebo or IV histamine-2 receptor antagonists.[4,5] Pooled data confirmed that the combination of endoscopy and pharmacologic treatment with a PPI reduced the need for repeated endoscopic therapy, surgical intervention, and blood transfusion.[6,7] This treatment strategy also proved to be more effective and less costly.[8-11]

The first study that attempted to use IV PPI in UGIB before endoscopic diagnosis was published by Daneshmend et al.[12] Although patients were randomized to receive an IV bolus injection of omeprazole or placebo, endoscopic therapy was offered at the discretion of the physician. In this study, IV PPI did not show any benefit in improving the outcome of the patients. In a placebo-controlled randomized study, our group studied the use of IV PPI before an endoscopy in the management of UGIB. We found that early PPI infusion on presentation reduced the number of patients with an actively bleeding ulcer on endoscopy.[13] The proportion of patients who required endoscopic therapy was reduced and the length of hospital stay was

Abbreviations: ICER, incremental cost-effectiveness ratio; IV, intravenous; PPI, proton pump inhibitor; UGIB, upper-GI bleeding; USD, US dollars.

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shortened in those who received a PPI. Meta-analysis pooling data on the clinical efficacy of a PPI initiated before an endoscopy with UGIB also confirmed that those who received a PPI were less likely to have stigmata of recent hemorrhage at the index endoscopy. Prior use of a PPI did not impact on the need for surgery and on mortality.[14]

Does the clinical benefit of reduced active bleeding on an index endoscopy justify the extra cost incurred for a wider use of IV PPI? Without a significant difference in the rate of recurrent bleeding, would the use of preemptive PPI still be cost effective? How would the cost-benefit be offset by the cost of an endoscopy and the cost of hospitalization?

This study was set to determine whether the early administration of high-dose omeprazole before an endoscopy in the management of UGIB would be cost effective. The analysis was based on the perspective of a clinical trial conducted in Hong Kong. To make the result from this study generalizable to other practices, a sensitivity analysis was applied to test the applicability of these data in other setting of hospital practices. The trial was also approved by the ethics committee of New Territory East Cluster Hospitals in Hong Kong.

PATIENTS AND METHODS

The present post hoc analysis was based on our previous randomized control trial that assessed the early administration of high-dose omeprazole infusion before an endoscopy in patients with UGIB.[13] Consecutive patients, who presented with overt signs of UGIB (ie, melena or hematemesis with or without hypotension) to the emergency department at the Prince of Wales Hospital, were evaluated by admitting residents for trial inclusions. Patients who were in hypovolemic shock (systolic blood pressure $<$90 mm Hg or a pulse rate $>$110 per minute) were initially resuscitated and then were considered for trial entry if their conditions stabilized. Those patients who were in refractory shock, pregnant, younger than 18 years old, or with a known allergy to PPIs were excluded.

Patients with various causes of UGIB were randomized to receive either omeprazole (a 80-mg IV bolus followed by 8 mg per hour) or placebo until the next planned endoscopy. A diagnostic endoscopy was offered within 24 hours. When patients were found to have an active bleeding ulcer or an ulcer covered with adherent clot, endoscopic therapy (epinephrine injection and heat probe thermocoagulation) was performed. Patients who had recurrent bleeding were offered a second attempt of endoscopic hemostasis. Surgery was used as a last resort for persistent bleeding despite medical and endoscopic therapy. All patients were observed for 30 days from the presentation of UGIB.

Capsule Summary

What is already known on this topic

- Endoscopic therapy is effective in controlling active bleeding in the upper-GI tract, and, in combination with high-dose IV infusion of proton pump inhibitors (PPI), it reduces recurrent bleeding.

What this study adds to our knowledge

- In a decision analysis of 631 patients with upper-GI bleeding, the use of high-dose IV PPI before endoscopy was shown to be an effective and cost-saving method of treatment, with the upfront increase in resources offset by the reduction in subsequent procedures and duration of hospital stay.

Decision analysis model in the management of UGIB

A decision analysis model that represented treatment pathways in the PPI group or the placebo group were constructed (Fig. 1). The cases of diagnostic endoscopy, endoscopic therapy, rebleeding, and a requirement of emergency surgery were counted. The final outcome would be either recovery from the bleeding episode and discharge from the hospital or the patient died from bleeding. This decision model measured the outcomes within 30 days after the presentation of UGIB.

Clinical data

A total of 631 patients were recruited from February 2004 to July 2005 (Table 1). In the omeprazole group, 187 patients (59.6%) had peptic ulcers, 125 (39.8%) had a nonulcer cause of UGIB, and 2 patients (0.6%) died before an endoscopy. In the placebo group, 190 patients (59.9%) had peptic ulcers, and 127 (40.1%) had a nonulcer cause of UGIB. Sixty patients (19.1%) in the PPI group and 90 patients (28.4%) in the placebo group required endoscopic hemostasis at an index endoscopy. The requirement of endoscopic therapy for the patients with nonulcer sources of bleeding between the PPI (5.7%) and placebo (6.3%) groups was not statistically different ($P = .87$). The relative risk of endoscopic therapy in all patients (ulcer and nonulcer) under PPI treatment versus a placebo was 0.67, 95% CI, 0.51-0.90. After endoscopic therapy, 4 of 60 patients (6.7%) in the PPI group and 6 of 90 patients (6.7%) in the placebo group had recurrent bleeding that required repeated endoscopic therapy. A total of 248 of 314 patients (79.0%) in the PPI group and 227 of 317 patients (71.6%) in the placebo group did not require endoscopic therapy, thus a reduction of 7.4%. The primary outcome in this cost-effectiveness comparison was the number of patients who averted endoscopic therapy within the follow-up period. We assumed that a preemptive PPI has no effect on the requirement of endoscopic therapy in patients without