Intravenous omeprazole after endoscopic treatment of bleeding peptic ulcers


**Question** Does omeprazole reduce the risk of recurrent bleeding after successful endoscopic treatment in patients with bleeding peptic ulcer?

**Design** Randomised double blind trial of 72 hours of intravenous omeprazole.

**Setting** A large university hospital in Hong Kong.

**Patients** A total of 240 patients with acute upper gastrointestinal bleeding endoscoped within 24 hours of admission and found to have a bleeding peptic ulcer in which bleeding was successfully controlled by endoscopic treatment.

**Intervention** Bolus injection of 80 mg intravenous omeprazole or identical placebo followed by infusion of omeprazole at 8 mg/hour or placebo for 72 hours. All patients were subsequently treated with oral omeprazole 20 mg daily for eight weeks, including one week of omeprazole, clarithromycin, and amoxicillin for patients who were CLO test positive.

**Outcome measures** The primary outcome measure was recurrent bleeding within 30 days. Secondary measures included blood transfusion requirement, need for surgery, duration of hospital stay, and overall mortality within 30 days.

**Results** Of 739 with peptic ulcer bleeding, 267 required endoscopic treatment which was unsuccessful in five; a further 19 were excluded because of life threatening concomitant illness, and three refused consent. Rebleeding occurred in eight (7%) of 120 randomised to intravenous omeprazole compared with 27 (23%) of 120 randomised to placebo infusion (relative risk of rebleeding with placebo 3.4 (95% confidence interval 1.6–7.1); p<0.001). Benefit was greatest within three days of admission when most rebleeding occurred. Patients receiving intravenous omeprazole had fewer units of blood transfused (p=0.04), a shorter duration of hospital stay (p=0.02), and fewer operations (p=0.14). After 30 days, five (4.2%) of those given intravenous omeprazole had died compared with 12 (10%) in the placebo group (p=0.13); none of the deaths in the omeprazole group were attributable to recurrent bleeding in contrast with six in the placebo group.

**Conclusion** After endoscopic treatment of bleeding peptic ulcers, high dose infusion of omeprazole substantially reduces the risk of recurrent bleeding.

**Comment** Active ulcer bleeding can usually be stopped by therapeutic endoscopy but 15–20% of patients rebleed, usually within the first 24 hours. The rebleeding rate is similar for all endoscopic haemostatic modalities and combinations of endoscopic treatments are little better than single modalities. Patients who rebleed have a high risk of dying. Rebleeding occurs as the blood clot which is formed over the arterial defect within the ulcer base is either dislodged or dissolves. It is clear that blood clot stability is dependent on intragastric pH and below 5, clot lysis occurs due to the combined effects of trypsin and acid. A pH greater than 6 is necessary for optimum platelet aggregation. Thus powerful acid suppressing drugs by stabilising the arterial plug have the potential to reduce rebleeding rates and thereby improve prognosis.

In 1992 Daneshmend and colleagues reported an extremely large randomised trial in which patients presenting acutely with gastrointestinal bleeding were administered intravenous boluses of omeprazole or placebo. The major end points of rebleeding and mortality were similar in both groups. This influential study persuaded the gastrointestinal community that omeprazole should not be used indiscriminately in all patients presenting with upper gastrointestinal bleeding. This conclusion is undoubtedly correct but it may not follow that acid suppressing drugs have no role in subgroups of patients. Eighty per cent of patients who present with acute gastrointestinal bleeding have an excellent prognosis without any type of intervention while at the other end of the spectrum a minority of patients will inevitably do badly because of massive bleeding or are unlikely to respond to any non-surgical therapy because they are dying from systemic disease. Thus acid suppressing drugs cannot be expected to have an impact in the majority of cases but the question arose as to whether in a subset of patients they may have a role. Close reading of the Daneshmend study showed that ulcer bleeding patients receiving omeprazole had a lower incidence of active bleeding than the placebo group at endoscopy, and although this did not translate into any differences in surgical operation rate or mortality, this trend is of interest. A criticism of this trial is that the drug regimen was insufficient to consistently increase gastric pH to at least 6.

Enthusiasm for the use of proton pump inhibitors was rekindled by a study from Khuroo and colleagues. In this trial bleeding ulcer patients were randomised to high dose oral omeprazole or matching placebo. Rebleeding rates (10.9 v 36.4%) and blood transfusion requirements were significantly reduced and mortality tended to be less in the omeprazole treated group. Cynics might criticise this trial
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