Canterbury District Health Board
Te Poari Hauora o Waitaha

Clinical Pharmacology Bulletin

Department of Clinical Pharmacology, Christchurch Hospital, Private Bag 4710, Christchurch

Medicines Information Service **Phone:** 80900 **Fax:** 80902
Medicines Utilisation Review **Phone:** 89971 **Fax:** 81003

March 2016 **No. 003/16**

Omeprazole use in Upper Gastrointestinal Bleeds

At the end of February this year all CDHB hospitals switched from using iv infusions of omeprazole to iv intermittent boluses in the treatment regimen for upper gastrointestinal bleeding. This decision (which involved General Surgery, Gastroenterology, Clinical Pharmacology, Pharmacy and the Emergency Department) was based on a recent meta-analysis that indicated no loss of efficacy when omeprazole iv was given intermittently rather than continuously. Hospital HealthPathways will be updated shortly. This bulletin outlines the use of omeprazole, including how to prescribe it, for this indication and presents the new guideline.

Mechanism of action

Omeprazole, and other proton pump inhibitors (PPIs), inhibit gastric acid secretion. It is a prodrug; following absorption into the systemic circulation it is protonated to its active form in parietal cells. This then binds to proton pump H+-K+-ATPase which is an enzyme expressed in parietal cells blocking hydrogen ion secretion into the gastric lumen and consequently increasing gastric pH.

Upper gastrointestinal bleeds

Following endoscopic therapy primary haemostasis is achieved in 90% of cases but re-bleeding occurs in 10-30% of these. Intravenous omeprazole is used to reduce bleeding pre-endoscopy (so making successful endoscopic therapy more likely) and to prevent re-bleeding post-endoscopic therapy. Coagulation and platelet aggregation in the upper gastrointestinal tract are highly dependent on gastric pH and both are inhibited at pH < 6.8 inhibiting clot formation. Low pH also promotes clot lysis and impairs healing. Maintaining a high gastric pH during and immediately post upper gastrointestinal bleeds has been shown to reduce the incidence of re-bleeds.

Evidence of efficacy

Until recently the evidence suggested that the maintenance of high gastric pH (> 6) is best achieved with a bolus injection of omeprazole followed by a continuous infusion for 72 hours. A recent meta-analysis (Sachar et al JAMA Intern Med. 2014; 174 (11) :1755-1762) found that intermittent omeprazole bolus injections were non-inferior to continuous infusions (risk ratio of intermittent bolus vs continuous infusions was 0.72 for re-bleeding within 7 days). A review of CDHB upper gastrointestinal bleeding guidelines has resulted in a change of practice away from continuous infusions to the use of intermittent boluses instead.

Oral PPI therapy for 4 to 8 weeks is usually sufficient for ulcer healing. PPI therapy should be reviewed after this period of time taking into consideration individual risk of re-bleeding, indications for continuing omeprazole and risk of adverse effects. The dose used is usually 20 mg once a day unless the patient is at very high risk of rebleeding, when higher doses may be beneficial e.g.
40 mg once or twice a day. A small audit carried out at the end of 2014 showed that 7 out of 8 patients studied received high oral doses (40 mg twice a day) post iv therapy, with only one receiving the recommended 20 mg once a day.

Adverse effects

PPIs are not as safe as they were once thought. Long term use of PPIs increase the risk of Clostridium difficile, pneumonia, hypomagnesaemia, hyponatraemia, interstitial nephritis and osteoporosis leading to hip fracture. This warrants prescribing the lowest effective dose and regular review of PPIs to consider discontinuation if appropriate. Rebound acidity can occur therefore it is important to taper PPI dosage prior to stopping therapy and to ensure alternative treatment, such as antacids is available if rebound acidity occurs. Patients should be educated about this.

New upper gastrointestinal bleeding regimen:
a) Bolus omeprazole IV injection: **80 mg stat**
Followed in 6 hours by

b) Omeprazole IV injection **40 mg every six hours.** The total duration of IV treatment should be 72 hours.

c) Omeprazole oral **20 mg once a day** should be commenced at the end of the IV treatment period in patients who do not have endoscopic features of a very high risk of re-bleeding. In those with a very high risk of rebleeding, higher doses may be beneficial e.g. 40 mg once or twice a day.

The patient criteria remain the same:
Use of this regimen should be considered in the following patients:

1. Following endoscopy in those with a peptic ulcer described by one of the classifications below:

Type of Bleeding	Endoscopic Features
Active	Spurting or Oozing bleed
Recent	Visible vessel or Adherent blood clot

2. Prior to endoscopy in those who are admitted with a history and findings that are strongly suggestive of an active upper GI bleed, such as:
   a. Observed haematemesis and/or melaena
   Plus either of:
   b. Cardiovascular instability (shown by HR>100, BP <100mm Hg systolic, or a postural drop of more than 15mm Hg systolic).
   OR
   c. Significant anaemia on FBC

Charting

The pre-printed IV continuous infusion of omeprazole chart (C160066) will no longer be used. Charting of the stat dose and the intermittent boluses will now be on the Drug Treatment Chart or in MedChart where available.

Summary

- Intermittent IV boluses of 40 mg every six hours are as effective as IV continuous infusions
- Continuous infusions of omeprazole are no longer used within CDHB hospitals
- Charting will now be on the medication chart
- Hospital HealthPathways will be updated shortly to reflect this change in practice
- The post iv infusion oral dose should be 20 mg