Canterbury District Health Board
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Clinical Pharmacology Bulletin

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May 2015 No. 004/15

Omeprazole use in Upper Gastrointestinal Bleeds

In the period January to March 2015 the use of oral and intravenous omeprazole at Christchurch Hospital was ~ 468 g and ~ 71 g respectively. The oral use was split between 10 mg capsules (~ 4 g), 20 mg capsules (~ 306 g), 40 mg capsules (~ 113 g) and oral liquid (~45 g). The intravenous use was split between the infusion (~ 26 g) and the injection (~ 45 g). Anecdotally, patients who have experienced a gastrointestinal bleed requiring a 70 hour intravenous omeprazole infusion are being prescribed inappropriately high oral doses on discontinuation of the infusion and on discharge. The following is a refresher on the use of omeprazole in this setting and a report of a recent small audit.

Pharmacology

Omeprazole and other proton pump inhibitors (PPIs) inhibits gastric acid secretion. It is a prodrug, is first absorbed into the systemic circulation then accumulates in parietal cells where it is protonated to its active form. This then binds to proton pump H^+-K^+-ATPase which is an enzyme expressed in parietal cells. Through this binding, hydrogen ion secretion into the gastric lumen is blocked and gastric pH is increased.

Upper gastrointestinal bleeds

These can be treated successfully with endoscopic therapy. Primary haemostasis is achieved in 90% of cases but re-bleeding occurs in 10-30% of these. It is in the prevention of re-bleeding post-endoscopic therapy that intravenous omeprazole is most commonly used. Coagulation and platelet aggregation in the upper gastrointestinal tract are highly dependent on gastric pH and both are inhibited at pH < 6.8. Low pH also inhibits clot formation, 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 however (Sachar et al JAMA Intern Med. 2014; 174 (11) :1755-1762doi:10.1001/jamainternmed.2014.4056) 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 is about to commence.

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 and indications for continuing omeprazole.

Risks associated with long term use of PPIs include gastrointestinal infections including *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 is available if rebound acidity occurs such as antacids. Patients should be educated on this.

Current upper gastrointestinal bleeding regimen:

1. Bolus omeprazole IV injection: 80 mg stat loading dose

Followed immediately by:

2. Continuous omeprazole IV infusion: 8 mg/h for 70 hours.
3. Oral omeprazole 20 mg once daily should be commenced at the end of the 70-hour infusion period.

Recent audit

Aim: To describe use of oral omeprazole prescribed after the continuous omeprazole IV infusion in surgical patients following upper gastrointestinal bleeds.

Method: Data on surgical patients given omeprazole infusions for upper gastrointestinal bleeding were collected over a month in November and December 2014. Data collected included oral doses immediately after the end of the continuous infusion. The ongoing plan i.e. duration of therapy, dose prescribed on discharge, instructions to the GP on discharge and dose prior to admission were gathered for each patients from the discharge summary in Health Connect South and the dispensing database (Health One). The doses prescribed were then compared to 20 mg once a day as recommended in the upper gastrointestinal bleeding guidelines and in the Blue Book.

Results:

	No. of patients
Total	8
Dose prescribed	
20 mg once daily	1
40 mg twice a day	7
Patients prescribed 40 mg twice a day:	
Dose prior to admission	
none	4
40 mg twice a day	1
20 mg twice a day	1
20 mg once daily	1
Duration prescribed on discharge	
3 months	3
1 month	2
6 weeks	1
continued on regular dose	1
Review on discharge instructions	
none	2
after 3 months	2
after 6 weeks	1
in the future	1
reduce to 40 mg once daily in 1 month	1

Conclusions

Omeprazole use post upper gastrointestinal bleeds may change shortly from continuous infusion to intermittent bolus injections. The post iv infusion oral dose should be 20 mg once daily as outlined in local guidelines. This small audit shows that inappropriately high oral doses were prescribed on discharge to at least 50% of patients and 25% had no review plan.