

# Use of proton pump inhibitors in upper gastrointestinal bleeding

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**TITLE** Omeprazole before endoscopy in patients with gastrointestinal bleeding

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**LIST OF ABBREVIATIONS** Confidence interval (CI), gastrointestinal (GI), non-steroidal anti-inflammatory drug (NSAID), proton pump inhibitor (PPI)

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**DECLARATION OF INTERESTS** No conflict of interests declared.

## SUMMARY

A randomised, double blind, placebo controlled trial was performed, enrolling 638 patients with overt signs of upper GI bleeding. Patients were excluded if they had refractory shock, age less than 18, allergy to PPI or those on long term aspirin for cardiovascular protection (this group of patients was included in another trial). Patients on other NSAIDs were included and there was no upper age limit.

Patients were randomised at admission to receive either omeprazole (80 mg bolus then infusion at 8 mg/hr) or a placebo infusion. The infusion was continued until endoscopy was performed (mean duration of infusion (+/-SD) was 14.7 +/-6.3 hours in the omeprazole group and 15.2 +/-6.3 hours in the placebo group).

At endoscopy, ulcers were treated (with adrenaline injection and heater probe), if indicated, until haemostasis was achieved. Adherent clots, if found, were removed. Omeprazole infusion was continued for 72 hours post endoscopy if therapy was employed.

The primary endpoint of the study was the need for endoscopic intervention at the first endoscopy.

Diagnosis of peptic ulcer was similar in both groups (59.6% in the omeprazole group and 59.9% in the placebo group).

Sixty out of three hundred and forty-one (19.1%) of patients in the omeprazole group compared to 90/371 (28.4%) in the placebo group required endoscopic therapy at the first endoscopy (risk ratio for the omeprazole group 0.67; 95% CI 0.51–0.90,  $p=0.007$ ). Statistically lower mean volumes of adrenaline were injected and a lower number of pulses of the heater

probe were used in the omeprazole group. Less actively bleeding ulcers and more clean-based ulcers were seen in the treatment group. No differences in the number of urgent endoscopies or episodes of shock prior to endoscopy were seen. Mortality rates, blood transfusion rates, need for surgical intervention and rebleeding rates within 30 days were also similar. Hospital stay, however, was significantly shorter in the omeprazole group (fewer than three days in 60.5% of patients in the omeprazole group, compared to 49.2% in the placebo group ( $P=0.005$ )). No adverse effects of omeprazole were seen.

## OPINION

It is already known that continuous PPI for 72 hours following endoscopic therapy reduces the risk of recurrent bleeding.<sup>1</sup> This has also been shown to save money<sup>2</sup> and is standard practice in the UK.

Blood clotting is optimal at neutral pH and is adversely affected in a lower pH environment, such as the stomach, due to increasing platelet instability and decreased availability of clotting factors.<sup>3</sup> High dose proton pump inhibition (such as the regimen used in the trial above) can result in a neutral pH environment in the stomach and enhanced coagulation.

Prior to the study described above, the role of PPI prior to endoscopy was not clear. A Cochrane meta-analysis in 2006<sup>4</sup> demonstrated a significant reduction in the proportion of patients with stigmata of recent haemorrhage at index endoscopy in patients treated with PPI, but did not show any effect on clinically important outcomes such as mortality, rebleeding or need for surgery.

This paper shows that high dose omeprazole infusion

prior to endoscopy reduces the likelihood of finding a bleeding peptic ulcer at first endoscopy thus significantly reducing the need for endoscopic therapy. Patients receiving omeprazole were more likely to have an ulcer with a clean base and more likely to go home earlier. This suggests that omeprazole facilitates clot formation over arteries in bleeding peptic ulcers, enhances clot stability and initiates ulcer healing.

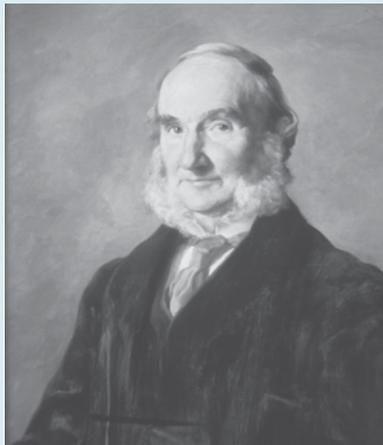
The implications of this study to UK practice are limited by geographical factors, in that the study was performed in Hong Kong. A recent survey of causes of upper GI

bleeding in the UK showed peptic ulcers as the cause in 33%<sup>5</sup> as opposed to 60% in the Hong Kong series. The other major drawback is that patients on low dose aspirin for cardiovascular protection were excluded from this trial. These patients tend to have more comorbidity and thus are at a higher risk of having adverse events when having an upper GI bleed.

Despite this, the benefits of omeprazole prior to endoscopy demonstrated by this trial provides reasonable evidence to support giving a high dose PPI infusion to patients presenting with an overt UGI bleed.

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### PAST PRESIDENTS

#### Professor Sir Alexander Russell Simpson (1835–1916)

Wherever he went he must have been asked if he was a relative of James Young Simpson, and if so what he thought of the latter's experiments with chloroform. In fact, Alexander

Russell Simpson was a nephew of the famous man, also educated in Bathgate Academy to the west of Edinburgh, and equally fascinated by, and committed to, midwifery, as it was still called.

After qualifying MD at Edinburgh in 1856, he was an assistant to his uncle for seven years before opting to be a GP, with a commitment to midwifery, in Glasgow's Blythwood Square. It is not known why he moved. Was it because his uncle expected too much of him? In addition to his own practice he was expected to assist with the care of James Young Simpson's hospital and private patients as well as teaching. He had to entertain the hundreds of distinguished international visitors eager to meet and pay homage to the great man.

When the old man died in 1870,

Alexander was appointed to succeed him in the Edinburgh Chair of Midwifery and Diseases of Women and Children, (an appointment that met with considerable disapproval in many quarters) serving for 35 years and eventually becoming Dean of the Medical Faculty.

Retiring in 1905, then knighted in 1906, he spent his retirement in evangelism, visiting mission hospitals in India and China of the United Free Church of which he had long been a member, and promoting temperance. Sadly he was killed in a road accident in a wartime blackout in 1916.

Derek Doyle  
*Obituaries Editor, The Journal RCPE*