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Is Prophylactic Intravenous Administration of a Proton Pump Inhibitor Necessary for Perioperative Management of Cardiac Surgery?


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ABSTRACT

Background: Mortality from gastrointestinal (GI) hemorrhage caused by antiplatelet or anticoagulant therapy (or both) is quite high after cardiac surgery. We previously reported that proton pump inhibitor (PPI) therapy is indispensable in preventing postoperative GI complications. PPIs are usually administered intravenously immediately after surgery and subsequently by oral formulations. We conducted a prospective study to evaluate whether intravenous PPI followed by oral administration is more efficient as prophylaxis than oral-only administration.

Methods and Results: We enrolled 40 patients scheduled to undergo coronary artery bypass grafting with cardiopulmonary bypass and randomly assigned them to receive oral PPIs alone (group 1) or intravenous PPI followed by oral administration (group 2). Postoperative upper GI endoscopy evaluations showed no evidence of GI bleeding. Only gastritis, esophagitis, and hiatal hernia were observed at similar incidences in the groups. Mean hospital stays were also similar, but the cost of PPI treatment was significantly lower in group 1.

Conclusion: No additional benefits of intravenous PPIs over oral formulations were demonstrated. Oral PPIs alone were effective and economical as prophylaxis against GI complications. Intravenous PPIs might be unnecessary in selected patients after cardiac surgery.

INTRODUCTION

Prophylaxis of gastrointestinal (GI) complications following cardiac surgery is considered mandatory because of the high mortality rate (11%-59%) with low morbidity (0.3%-2%) [D'Ancona 2003; Filsoufi 2007; Glance 2007; Rodriguez 2007]. The administration of postoperative antiplatelet or anticoagulant therapy (or both) and the concomitant use of nonsteroidal anti-inflammatory drugs as pain relievers reinforce the need for prophylactic treatment against GI bleeding and other complications [Hata 2005; Bhatt 2008].

Proton pump inhibitors (PPIs) are the most effective inhibitors of gastric acid secretion and are recommended for this purpose [Hata 2005; Bhatt 2008]. Intravenous PPIs are administered immediately after an operation, because most patients transferred to the intensive care unit are unconscious and intubated. After extubation and resumption of oral intake, intravenous PPIs are usually switched to oral PPIs. Improvements in perioperative management have shortened intubation times, and many patients can resume oral intake as early as several hours after an operation. We therefore studied whether intravenous PPIs are still necessary if oral PPIs can be administered within several hours after cardiac surgery.

MATERIALS AND METHODS

Consent to participate in this study was obtained from all patients, and the study protocol was approved by an institutional review board before initiation of the study and publication of the manuscript.

We enrolled 40 consecutive patients who were scheduled to undergo coronary artery bypass grafting with cardiopulmonary bypass (CPB). No patient had a previous history of GI disease. The patients were randomly divided into 2 groups: group 1 (n = 20), in which patients received only oral PPIs from the morning after surgery until discharge, and group 2 (n = 20), in which patients received intravenous PPIs for 3 days, from the day of surgery until postoperative day (POD) 2, followed by oral PPIs from POD 3 until discharge. The oral PPI rabeprazole was administered at a dosage of 10 mg once daily in the morning. No patient received oral PPIs on the day of surgery. The intravenous PPI omeprazole was administered at a dosage of 20 mg twice daily (40 mg/day), for a total of 6 times until POD 2. The first dose of intravenous PPI was administered at the time of skin incision, the second dose was administered on transfer to the intensive care unit after surgery, and the third dose was administered on the morning of POD 1. Then, intravenous PPI was given 3 more times at 12-hour intervals (Table 1). All patients received 100 mg acetylsalicylic acid and 200 mg ticlopidine daily as postoperative antiplatelet therapy from POD 1. Upper GI

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endoscopy (UGIE) examination was performed in all patients between POD 5 and POD 7, regardless of the presence or absence of abdominal symptoms.

Statistical analyses were performed with StatView software (version 5.0; SAS Institute, Cary, NC, USA). Groups were compared with the Student t test and the Pearson chi-square test. A 2-tailed *P* value <.05 was considered to indicate statistical significance.

Table 1. Proton Pump Inhibitor Regimen*

Patient Group	Regimen/Cost	Day of Operation	PODs 1 and 2	PODs 3+
Group 1	Rabeprazole, doses/d	0	1	1
	Omeprazole, doses/d	0	0	0
	Cost, yen/d	0	231.8	231.8
Group 2	Rabeprazole, doses/d	0	0	1
	Omeprazole, doses/d	2	2	0
	Cost, yen/d	1340	1340	231.8

*POD indicates postoperative day.

RESULTS

The mean age of the 40 patients (32 men and 8 women) was 64.2 years (range, 44-78 years). There were no significant differences between the groups in preoperative clinical characteristics (Table 2).

Table 2. Preoperative Profiles of Patients

	Group 1 (n = 20), n	Group 2 (n = 20), n	*P*
Male sex	15 (75%)	17 (85%)	NS*
Diabetes mellitus	7 (35%)	9 (45%)	NS
Hypertension	15 (75%)	16 (80%)	NS
Hyperlipidemia	14 (70%)	13 (65%)	NS
Smoking	12 (60%)	11 (55%)	NS

*NS indicates not statistically significant.

The mean CPB time was 106.6 minutes in group 1 and 104.8 minutes in group 2 (nonsignificant). The peak postoperative creatine kinase MB isoenzyme level was 24.6 IU/L in group 1 and 25.1 IU/L in group 2 (also nonsignificant). These results indicated that the 2 groups were similar with respect to the invasiveness of the surgeries.

All patients were extubated on the day of surgery and resumed oral intake no later than several hours after the operation. No patient reported any abdominal symptoms during their hospital stay. Their hemodynamics were stable without any serious complications.

The results of UGIE examinations were similar in the groups (Table 3). No evidence of active GI bleeding was seen; however, other noncritical GI findings, such as superficial gastritis, erosive gastritis, esophagitis, and hiatal hernia, were observed in 21 (52.5%) of the patients, even though all patients remained asymptomatic.

The 2 groups had similar mean hospital stays (group 1, 9.8 days; group 2, 9.8 days). The mean cost of the PPI therapy was significantly lower in group 1 than in group 2 (2549.8 yen and 3882.6 yen, respectively; $P = .012$).

Table 3. Upper Gastrointestinal Endoscopy and Overall Results*

	Group 1 (n = 20), n	Group 2 (n = 20), n	*P*
Superficial gastritis	2 (10%)	2 (10%)	NS
Erosive gastritis	1 (5%)	2 (10%)	NS
Esophagitis	2 (10%)	3 (15%)	NS
Hiatal hernia	4 (20%)	5 (25%)	NS
Active ulcer	0 (0%)	0 (0%)	NS
Total	9 (45%)	12 (60%)	NS
Mean hospital stay, d	9.8	9.8	NS
Mean PPI cost, yen	2549.8	3882.6	.021

*NS indicates not statistically significant; PPI, proton pump inhibitor.

DISCUSSION

Although the pathogenesis of postoperative GI complications is complex and multifactorial, perioperative visceral hypoperfusion appears to play a key etiologic role. Several preoperative factors that can contribute to visceral hypoperfusion, including advanced age, low cardiac function, coexisting peripheral vascular diseases, and renal failure, carry an increased risk of postoperative GI complications [Zacharias 2000; Filsoufi 2007].

PPIs are recommended to reduce the risk of GI bleeding associated with antiplatelet or anticoagulant therapy (or both) [Hata 2005; Bhatt 2008]. These drugs can be administered either orally or intravenously, and the efficacies of the 2 routes of administration have been reported to be equivalent [Javid 2009]. The costs are quite different, however. We used 40 mg/day omeprazole (1340.0 yen/day) as the intravenous PPI and used 10 mg/day rabeprazole (231.8 yen/day) as the oral PPI. In general, intravenous PPIs are approximately 6 times more expensive than oral PPIs.

We conducted UGIE examinations in all patients to evaluate the postoperative status of the GI tract, regardless of the presence or absence of abdominal symptoms. Postoperative abdominal symptoms are occasionally subjective and can be attributed in part to mood disturbances caused by various types of physiological and psychological stresses [Hata 2006]. Some GI complications were not detected in our previous studies until UGIE examinations were performed [Hata 2005, 2006]. Most upper GI complications occur within 7 days after cardiac surgery [Aranha 1984]. Therefore, all patients were scheduled to undergo UGIE examination between POD 5 and POD 7.

No active bleeding was observed in this study, even though all patients received combined antiplatelet therapy from POD

1. Previous studies have reported a 0.35% to 5.7% incidence of GI bleeding after cardiac surgery despite the use of prophylactic antacid agents other than PPIs [Halm 2000; van der Voort 2000; Hata 2005], albeit the patients' characteristics in these studies differed considerably. Although UGIE findings might have been present before surgery, the incidence of gastroesophagitis (including superficial gastritis, erosive gastritis, and esophagitis) was 30% in our study, which is within the previously reported range of 12.2% to 68.0% [Zacharias 2000; D'Ancona 2003; Hata 2005, 2006]. Up to 52.5% of the patients had insidious gastroesophagitis and hiatal hernia, even during sufficient PPI therapy. These results may support the efficacy and use of PPI therapy.

The results of our study provided no evidence suggesting that the additional use of intravenous PPIs is superior to oral PPIs alone. The 2 groups did not differ significantly with respect to the incidence of GI findings. Only the mean costs were significantly different; the UGIE findings and durations of hospitalization were similar. Our results suggest that oral PPIs alone may suffice as prophylactic agents if they can be started by the morning after surgery. Cost-effectiveness should also be taken into account, because the purpose of PPI therapy is prophylaxis.

Our study had several important limitations, and our results cannot simply be extrapolated to all patients. First, the number of the patients was quite small. The patient population also seemed to be skewed toward a younger mean age and a higher proportion of men. Advanced age is a proven risk factor for postoperative GI complications [Zacharias 2000; Filsoufi 2007; Rodriguez 2007]. Second, the patients' conditions were stable perioperatively. No patient had a history of GI diseases, and all had an unremarkable perioperative course. All patients were extubated on the day of surgery and resumed oral intake no later than several hours postoperatively. Prolonged mechanical ventilation is a strong determinant of GI complications [Halm 2000; D'Ancona 2003]. Other operative conditions and perioperative complications, such as procedure urgency, prolonged CPB time, concomitant valve procedure, renal failure, sepsis, sternal infection, and hemodynamic instability requiring high doses of inotropic agents or intra-aortic balloon pumping are also proven risk factors [Zacharias 2000; D'Ancona 2003; Filsoufi 2007; Rodriguez 2007]. The occurrence of such perioperative complications might lead to different outcomes.

CONCLUSION

A combined regimen of intravenous and oral PPIs can be replaced by a regimen of oral PPIs alone in selected patients, with no loss of efficacy. Oral PPIs alone provided effective prophylaxis and were superior in this study in terms of cost-effectiveness. Patients with complicated perioperative conditions and courses should be managed individually.

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