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Effect of Preoperative Intravenous Pantoprazole in Elective-Surgery Patients: A Pilot Study

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Abstract

Background—This study evaluated the effects of intravenous pantoprazole on gastric volume and acid output in elective-surgical patients.

Methods—This is a multicenter, randomized, pilot study of adult patients receiving intravenous pantoprazole: 40 mg every 24 h, 40 mg every 12 h (q12h) or 80 mg q12h. The first dose was administered 1 h before general anesthesia for surgery. All gastric fluid was aspirated through a nasogastric tube 1 h before dosing and through the postoperative period. Aspirate volume was recorded; pH and H⁺ concentrations were measured.

Result—Twenty-six patients were enrolled and 21 were evaluable. Pantoprazole was well tolerated. All regimens decreased gastric acid output and volume, and increased pH within 1 h of dosing. Effects were sustained for up to 12 h following single-dose administration.

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Conclusions—Intravenous pantoprazole administered prior to anesthesia induction may be efficacious for the reduction of gastric volume and acid output, and for pulmonary aspiration prophylaxis in surgical patients.

Keywords

Intravenous; Pantoprazole; Aspiration pneumonia; Gastric volume; Gastric acid output

Introduction

Aspiration of gastric contents at the time of anesthesia induction is a rare but serious complication that can lead to pulmonary morbidity and death in the perioperative period [1–3]. Patients at increased risk of gastric aspiration include children, the elderly, those undergoing emergency operations and abdominal surgery, and those with a history of delayed gastric emptying [1–3]. It has been demonstrated that a gastric pH of <2.5 and a gastric volume of >25 ml/h increases the risk of aspiration pneumonia [3, 4]. Several studies suggest that the risk of aspiration pneumonia is increased even at a pH of 3.5 [5–7]. Thus, increasing gastric pH and decreasing gastric volume may reduce the incidence of gastric content aspiration in patients undergoing surgery.

The efficacy of pantoprazole, a proton pump inhibitor given intravenously to suppress gastric acid secretion in patients with hypersecretory conditions such as Zollinger-Ellison syndrome (ZES) and in patients with gastroesophageal reflux disease (GERD), is well established [8–11]. Antisecretory agents, including the H₂-receptor antagonists and proton pump inhibitors, are also effective in increasing gastric pH and decreasing gastric volume in patients undergoing various surgical procedures, such as cesarean sections, general surgery, and gynecologic, lower abdominal, orthopedic, dental or ear/nose/throat operations [6, 12–25]. Although potent acid suppressants are often used in obstetrical emergencies, there are no defined guidelines according to which these agents can be used in this or other perioperative settings [26]. Also, the timing of administration of these agents relative to surgery onset is not well defined. In elective-surgery patients, one study found that either intravenous pantoprazole or the H₂-receptor antagonist ranitidine given 1 h before surgery was effective in reducing gastric volume and increasing gastric pH [25].

To address the value of using an intravenous proton pump inhibitor to reduce the risk of aspiration, the primary objective of the current study was to assess the effect of three dosing regimens of intravenous pantoprazole on gastric acid output, gastric volume, and gastric pH in patients undergoing major elective surgery. Secondary objectives included assessing the difference between a 2- and 15-min infusion rate and the effect of intravenous pantoprazole on the risk of aspiration pneumonia.

Methods

Setting

This was a randomized, parallel-group, single-blind (blinded to the physician, who assessed safety), pilot study conducted in patients undergoing major elective surgery at eight US

centers between October 2000 and November 2002. The study protocol was approved by the institutional review board at each site and was conducted according to the Declaration of Helsinki.

Study Drug

A 40 mg dose of pantoprazole for intravenous injection was provided as a lyophilized powder formulation in open-label, sealed glass vials. Doses were prepared for infusion by the pharmacy at the study site by reconstitution with normal saline.

Patients

All patients provided written, informed consent. Patients eligible to participate in the study included men or non-pregnant women aged 18–76 years who were undergoing elective, nontransplant, abdominal surgery (that did not affect the esophagus/stomach or duodenum above the ligament of Treitz) lasting between 2 and 10 h from incision to closure, and who would otherwise undergo the routine placement of a nasogastric (NG) tube for 24 h. Only those patients who had an anticipated endotracheal intubation for <24 h after discharge from the operating room and likely uncomplicated recovery were enrolled in the study.

Additionally, study participation required that the patients be able to tolerate the insertion of an NG or orogastric (OG) tube without sedation and remain without any food by mouth [nil per os (NPO)] for the duration of the study. Patients were required to have a gastric aspirate pH of ≥ 3.0 in at least one of four aliquots of the baseline collection to ensure acid-secreting capability.

Patients excluded from study enrollment were those with any clinical signs/symptoms of aspiration pneumonia on screening chest X-ray or those with presence of grossly bloody or coffee-ground material in NG/OG tube aspirate prior to surgery. Additionally, patients were excluded if they had significant acute and/or concurrent medical diseases; history of or current upper gastrointestinal bleed, erosive esophagitis, peptic ulcer disease (within the past year), transplant surgery, ZES or other severe/serious hypersecretory condition; history of vagotomy; and those who had vascular surgery (except small uncomplicated aortic aneurysm repair). Patients with metastatic malignancy, except those with localized liver metastasis with normal liver function tests, were excluded (localized cancers were permitted), as well as those with a history of, or current, eye disorders that required continuing medical therapy. Patients who had a history of substance abuse or who had had treatment for alcohol abuse within the year prior to enrollment were excluded. Additionally, only 25% of enrolled patients (nine patients) were positive for *Helicobacter pylori* at screening; thus, any patient beyond this number was excluded from the study. Patients were excluded from study entry if they had used H₂-receptor antagonists, gastrointestinal promotility drugs, or sucralfate within 24 h of planned surgery or proton pump inhibitors within 72 h of surgery. Any patient who was exposed to an investigational drug or investigational dosage of other marketed drugs within 30 days of the screening visit was excluded from the study.

Study Design

Patients were randomized to receive pantoprazole following one of six treatment regimens: 40 mg every 24 h (q24h), 40 mg (q12h), or 80 mg q12h, each given as a 2- or 15-min

infusion for up to 72 h. Patients were NPO after midnight prior to the day of surgery. On the day of surgery and before sedation, patients had an Anderson 16 or 14 French NG/OG tube inserted. Tube placement in the stomach was verified by auscultation while injecting air through the tube and by recovery of >90% of infused water. Stomach contents were evacuated prior to beginning aspirate collection for the determination of basal acid output (BAO). Gastric secretions were collected at 15-min increments for 1 h prior to infusion of the study drug to assess the patient's BAO; the pH of these initial aspirates was also measured.

The first infusion of the study drug was started approximately 60 min (± 30 min) prior to the induction of anesthesia. Subsequent doses were administered every 12 or 24 h depending on the patient's treatment assignment. The study drug was to be administered for 24 h. However, some patients terminated treatment after one dose. After the start of infusion, all gastric secretions were collected until the induction of anesthesia (minimum of two samples taken every 15 min). After the induction of anesthesia and throughout surgery, all gastric secretions were collected every 30 min for the first 12 h and then at 1-h intervals until the NG/OG tube was removed. Each gastric collection was analyzed for gross appearance (color and presence or absence of coffee grounds) and volume. Occult blood testing was performed on gastric samples as necessary (Gastrocult®, SmithKline Diagnostics). Samples were then frozen and sent to a central laboratory for measurement of pH and H^+ ion concentration $[H^+]$ and calculation of acid output (acid output = $[H^+] \times \text{volume}$).

If clinical signs of pneumonia were present, a sputum specimen was obtained and cultured, and an antibiotic sensitivity analysis was performed. For consistent evaluations, all patients received prophylactic antibiotic treatment during the pre-, peri-, and postoperative periods. A diagnosis of pneumonia required the following: radiographic findings of a new or evolving infiltrate(s) not related to another disease process; fever defined as an oral temperature of $>38^\circ\text{C}$, a tympanic temperature of $>38.5^\circ\text{C}$, a rectal/core temperature of $>39^\circ\text{C}$, or hypothermia defined as a rectal/core body temperature of $<35^\circ\text{C}$; and a white blood cell (WBC) count of $>10,000/\text{mm}^3$, 15% immature neutrophils (bands) regardless of total peripheral WBC count, or leukopenia ($\text{WBC} < 4,500/\text{mm}^3$). In addition, a diagnosis of pneumonia required the presence of at least three of the following: (1) new or increased cough, (2) new onset of purulent sputum production or respiratory secretions or a change in the character of sputum, (3) auscultatory findings on pulmonary examination of rales and/or evidence of pulmonary consolidation (dullness on percussion, bronchial breath sounds or egophony), (4) dyspnea, tachypnea, or a respiratory rate of >20 breaths/min, particularly if any or all of these were progressive in nature, (5) hypoxemia with a PaO_2 of <60 mmHg (as determined by arterial blood gas), an oxygen saturation of $<90\%$ (as determined by pulse oximetry) while the patient was breathing room air, or respiratory failure requiring mechanical ventilation, (6) tachycardia of >90 beats per minute, (7) pleuritic chest pain, and (8) new or worsened confusion.

Patients were instructed not to discuss their dose or dose frequency with the designated safety physician at each study site, who was blinded to patients' treatment assignments. Patients were monitored for up to 2 days during the period of hospitalization (the treatment period), for 48 h following the last dose of the study drug (the short-term follow-up period),

and for 30 days if they had experienced a serious adverse event (long-term follow-up period). Patients were withdrawn at any time if they were unable to remain in the study for 24 h postoperatively or if they experienced a clinically significant upper gastrointestinal bleeding episode. Patients were allowed to withdraw from the study at any time and for any reason. If patients were withdrawn from the study prematurely, the investigator documented the reason for the withdrawal and conducted a complete clinical evaluation. If a patient withdrew due to an adverse event (AE), the principal investigator followed the patient until resolution of the AE.

Patients were allowed to use oral antacids up to the start of the NPO period. Any medications considered essential to the patients' welfare were continued during the study period, except for oral antacids, proton pump inhibitors other than the study drug, H₂-receptor antagonists, sucralfate, and gastrointestinal promotility drugs. All medications taken within 1 month of study entry and throughout the study were recorded.

Outcome Measures

Primary efficacy end points were the assessment of hourly gastric acid output, volume, and pH. In post hoc analysis, gastric volume and pH were used to assess the risk of aspiration pneumonia. Specific criteria used as surrogates for the risk of aspiration pneumonia included the following: (1) gastric aspirate volume of >25 ml/h, (2) 1 gastric aspirate pH measurements of <2.5, (3) 1 gastric aspirate pH measurements of <3.5, (4) 1 gastric aspirate pH measurements of <2.5 or volume of >25 ml/h, and (5) 1 gastric aspirate pH measurements of <3.5 or volume of >25 ml/h. These criteria were applied to gastric aspirates collected at baseline and during each of the first three hours following study drug administration. In addition, chest X-rays were performed and signs and symptoms of pneumonia were evaluated at 48 h after the last dose of the study drug to monitor for the presence of pneumonia. The specific clinical, radiological, and microbiologic criteria detailed above were required to confirm a diagnosis of pneumonia.

Safety Analysis

Safety was monitored by complete physical examination, vital signs, and clinical laboratory evaluations. All patients underwent continuous clinical, laboratory, and other special monitoring procedures as mandated by their underlying condition and surgical procedure. Although any pneumonia cases that occurred during the treatment and short-term follow-up periods were considered an outcome measure, cases of pneumonia that occurred after the 48-h chest X-ray and during the 30-day period following the last dose of the study drug were recorded as an AE. A fundoscopic evaluation was performed at baseline and again at 48 h after the last dose of the study drug.

Statistical Analyses

A signed rank test was performed to assess the changes from baseline for the hourly volume, gastric pH, and acid output. Median values were compared to assess the effect of the dose regimen and infusion duration. The changes from baseline in volume, gastric pH, and acid output were compared between the 40 and 80 mg groups over the first 12 h using a Student's *t*-test on the ranks of the changes from baseline.

Results

Patients

Patient randomization and baseline demographics are summarized in Fig. 1 and Table 1, respectively. A total of 26 patients were enrolled, with 21 patients included in the modified intent-to-treat analysis (MITT). The MITT analysis excluded five patients who did not have a gastric aspirate pH of ≥ 3.0 in at least one of four aliquots during the baseline period. The study was discontinued prematurely due to slow enrollment. All patients were included in the safety analyses. Four patients discontinued the study prematurely, one due to an AE (bleeding after placement of the NG tube) and three due to protocol violations. All patients underwent elective abdominal surgery, with a mean procedure duration of 5.2 h. Seventeen patients (65.4%) had colonic resection (partial or hemicolectomy) and three patients had ventral hernia repair (one of whom also had a transurethral resection of the prostate). The remaining eight patients had the following procedures: subtotal colectomy, removal of an insulinoma, exploratory laparotomy with lysis of adhesions, Whipple procedure, resection of a pelvic sarcoma, and liver wedge resection. A total of 24 patients were taking one or more medications prior to study entry, and all patients received concomitant medications during the study, most commonly anesthetics, analgesics, antibiotics, and anticoagulants.

Efficacy

The effect of the dosing regimen (40 mg q12h versus 40 mg q24h versus 80 mg q12h) on gastric acid output, volume, and pH is shown in Fig. 2. Although the sample size was too small to allow statistically meaningful comparisons, the figure shows that gastric volume and acid output declined and gastric pH increased in all three groups during the first hour after administration of the study drug. The antisecretory effect was even more pronounced during the second hour following pantoprazole administration, and by the third hour median acid output was zero and gastric volume was minimal. The antisecretory effect continued through the end of the gastric aspirate collection period in all groups.

Data for the 40 mg groups were pooled, as were all data for the 80 mg groups, during the first 12 h after study drug administration, in order to perform statistical comparisons of the effect of the initial dose on gastric acid output and volume (Fig. 3). Both the 40 mg and the 80 mg doses of pantoprazole significantly lowered gastric acid output and volume at all time points ($P < 0.023$ and $P < 0.008$, respectively) compared with baseline, except for the 1-h time point in the 80 mg group by gastric volume measure. There were no significant differences between the two doses at any time point.

The effect of the infusion rate (2 versus 15 min) during the first 12 h on gastric acid output is illustrated in Fig. 4; because the two 40 mg groups (every 12 h and every 24 h) received the same dose over the first 12 h, data from these two groups were combined. The infusion rate did not markedly affect the gastric acid output, gastric acid volume, or pH.

The percentage of patients who were at risk of aspiration pneumonia using criteria of a pH of < 2.5 or volume of > 25 ml/h is shown by treatment group in Fig. 5. All patients in the MITT population met at least one criterion for risk of aspiration pneumonia prior to infusion of the first pantoprazole dose. During the first hour, approximately two-thirds of the patients

had a gastric pH of <2.5 or volume of >25 ml/h. During the second hour, only 29% of patients met these risk criteria. By the third hour, no patients met either risk criterion.

When using aspiration risk criteria of a gastric pH of <3.5 or volume of >25 ml/h, 86% of patients experienced one of these risk criteria during the first hour (data not shown). During the second hour, this percentage decreased to 29%, and by the third hour only 9.5% of patients had a gastric pH of <3.5 or volume of >25 ml/h; no patients met either risk criterion by the seventh hour. Although a greater percentage of patients receiving the 80 mg dose reached the critical thresholds for risk reduction for aspiration pneumonia earlier than patients receiving 40 mg pantoprazole, the sample size was too small to draw definitive conclusions regarding the optimal dose. None of the patients had signs or symptoms of pneumonia at the 48-h follow-up assessment.

Safety

A total of ten patients (38.5%) reported a total of 22 AEs during the study period. Of these, eight patients reported 16 AEs that were definitely not related to study drug as determined by the investigator; one patient reported two AEs that were possibly related to the study drug (confusion, anxiety); and one patient reported four AEs that were probably related to the study drug (nausea, headache, salivation, abnormal taste). The most commonly reported AEs included nausea, pyrexia, and anxiety. One patient in the 80 mg group discontinued the study due to an AE (blood in the gastric aspirate due to trauma associated with NG tube placement). There were three patients with serious AEs, none of which was considered related to the study drug. No deaths occurred during the study, and there were no clinically important changes in vital signs, laboratory evaluations, or physical examinations. No patients had any signs of optic-nerve swelling or disc pallor, and the disc size was equal bilaterally for all patients at each assessment.

Discussion

The results of this study show that in NPO elective-surgery patients, both the 40 and 80 mg dose of intravenous pantoprazole decreased gastric acid output, lowered gastric volume below 25 ml/h, and raised gastric pH above 2.5. The reduction of gastric acid output and volume and increase in pH were evident within the first hour after study drug administration. These results suggest that the risk of aspiration was reduced during the first hour following study drug administration and was further reduced in the third hour.

Although a pH of <2.5 is cited most often in the literature as the threshold for increased risk of aspiration pneumonia, there is evidence that pneumonitis can occur after inhalation of gastric material at a pH of 3.5 [5], and subsequent studies have used this more conservative criterion for assessing the risk of aspiration pneumonia [6, 7]. Using this criterion, 86% of patients had at least one gastric aspirate with a pH of <3.5 or volume of >25 ml/h within the first hour of drug administration. This was reduced to 29% in the second hour and 9.5% in the third hour. No patient developed pneumonia in this study, as prospectively defined.

A previous randomized, controlled trial conducted by Memis et al. [25] evaluated the effects of intravenous pantoprazole, ranitidine, and saline in patients undergoing elective surgery.

The findings of this study, similar to current study, showed that both pantoprazole and ranitidine administered 1 h prior to surgery significantly increased pH and decreased gastric volume compared with saline ($P < 0.0005$ for both comparisons). Other studies have evaluated the effect of other proton pump inhibitors on acid control and have found them to be effective in the perioperative setting [6, 12, 14, 16–18, 23, 27].

However, because the present study evaluated intravenous pantoprazole, the results can best be compared with other studies that have evaluated proton pump inhibitors using intravenous formulations. A study conducted by Rocke et al. evaluating the effect of intravenous omeprazole versus placebo in women undergoing emergency cesarean sections found that the addition of 40 mg intravenous omeprazole to an antacid regimen increased pH to above 3.5 ($P < 0.001$ compared with placebo) and lowered gastric residual volume at both intubation ($P = 0.006$ compared with placebo) and extubation ($P = 0.01$ compared with placebo) [6]. Another study by Tripathi et al. [16], also conducted in women undergoing emergency Cesarean sections, found that intravenous omeprazole increased gastric pH significantly more than intravenous ranitidine ($P < 0.05$), although the authors concluded that the difference between therapies was not clinically relevant. Atanassoff et al. [14] evaluated the effect of a single dose of intravenous omeprazole versus a single dose of intravenous ranitidine on gastric pH in patients undergoing lower abdominal surgery and found that 20 and 40 mg omeprazole increased gastric pH 2.5 after a median of 80 and 40 min, respectively. Patients receiving 25 or 50 mg intravenous ranitidine attained this same threshold at a median of 32 and 44 min, respectively [14].

Of note, the Atanassoff study evaluating omeprazole and ranitidine found that the optimal time to administer antisecretory agents is 30–45 min prior to surgery [14]. The study conducted by Memis et al. [12, 25] evaluating pantoprazole and ranitidine showed that the optimal time to administer these agents was 1 h prior to surgery. The present study was designed so that patients received their pantoprazole treatment assignment approximately 1 h prior to the induction of anesthesia. However, the results indicate that, although acid suppression was apparent during the first hour after surgery, the effect was more pronounced during the second hour. These data suggest that it may be beneficial to administer pantoprazole 2 h prior to the induction of anesthesia in order to attain maximum benefit within the first hour after onset of surgery; however, further study is required. Overall, the results of the present study are consistent with the above studies and add to the body of literature suggesting that intravenous proton pump inhibitors adequately control gastric acidity and, more importantly, reduce the risk of aspiration.

The current study has some limitations that should be considered. First, enrollment in the present study was slow, and the study itself was discontinued prematurely. Thus, the trial, which was designed as a pilot, was not adequately powered to make definitive conclusions regarding the effect of intravenous pantoprazole on the control of acid output or the risk of pneumonitis in patients during the perioperative period. Furthermore, there was no placebo control group, so only limited conclusions can be drawn regarding the effect of pantoprazole on acid suppression. However, in the previously discussed study by Memis et al. [25] intravenous pantoprazole was effective in increasing pH and lowering gastric volume compared with saline. Other studies have evaluated various other proton pump inhibitors

(including lansoprazole, omeprazole, and rabeprazole) against placebo in elective-surgery patients, and have shown that the effects of acid suppression are related to the study drug whether given intravenously or orally [6, 12, 17, 18, 23, 27].

In summary, the results of this study suggest that 40 or 80 mg intravenous pantoprazole administered prior to anesthesia induction may be efficacious for gastric volume and acid control and pulmonary aspiration prophylaxis in NPO surgical patients. In addition, intravenous pantoprazole was well tolerated in this patient population. As this was a pilot study, further investigation would be required to confirm the optimal dose.

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References

1. Olsson GL, Hallen B, Hambraeus-Jonzon K. Aspiration during anaesthesia: a computer-aided study of 185, 358 anaesthetics. *Acta Anaesthesiol Scand*. 1986;30:84–92. [PubMed: 3754372]
2. Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary aspiration during the perioperative period. *Anesthesiology*. 1993;78:56–62. doi:10.1097/0000542-199301000-00010. [PubMed: 8424572]
3. James CF, Modell JH, Gibbs CP, Kuck EJ, Ruiz BC. Pulmonary aspiration—effects of volume and pH in the rat. *Anesth Analg*. 1984;63:665–668. [PubMed: 6731893]
4. Roberts RB, Shirley MA. Reducing the risk of acid aspiration during cesarean section. *Anesth Analg*. 1974;53:859–868. [PubMed: 4473928]
5. Taylor G Acid pulmonary aspiration syndrome after antacids. A case report. *Br J Anaesth*. 1975;47:615–617. doi:10.1093/bja/47.5.615. [PubMed: 237522]
6. Rocke DA, Rout CC, Gouws E. Intravenous administration of the proton pump inhibitor omeprazole reduces the risk of acid aspiration at emergency cesarean section. *Anesth Analg*. 1994;78:1093–1098. doi:10.1213/00000539-199406000-00010. [PubMed: 8198263]
7. Atanassoff PG, Alon E, Pasch T. Effects of single-dose intravenous omeprazole and ranitidine on gastric pH during general anesthesia. *Anesth Analg*. 1992;75:95–98. doi: 10.1213/00000539-199207000-00018. [PubMed: 1616168]
8. Metz DC, Forsmark C, Lew EA, et al. Replacement of oral proton pump inhibitors with intravenous pantoprazole to effectively control gastric acid hypersecretion in patients with Zollinger-Ellison syndrome. *Am J Gastroenterol*. 2001;96:3274–3280. doi: 10.1111/j.1572-0241.2001.05325.x. [PubMed: 11774936]
9. Lew EA, Pisegna JR, Starr JA, et al. Intravenous pantoprazole rapidly controls gastric acid hypersecretion in patients with Zollinger-Ellison syndrome. *Gastroenterology*. 2000;118:696–704. doi: 10.1016/S0016-5085(00)70139-9. [PubMed: 10734021]
10. Metz DC, Pratha V, Martin P, et al. Oral and intravenous dosage forms of pantoprazole are equivalent in their ability to suppress gastric acid secretion in patients with gastroesophageal reflux disease. *Am J Gastroenterol*. 2000;95:626–633. doi: 10.1111/j.1572-0241.2000.01834.x. [PubMed: 10710049]
11. Pratha V, Hogan D, Lynn RB, Karlstadt R, Burton M, Metz DC. Intravenous pantoprazole is an effective gastric acid suppressant when used initially in patients with gastroesophageal reflux disease (GERD) Digestive Disease Week, New Orleans, Louisiana, USA, 5 15–20, 2004.
12. Memis D, Turan A, Karamanlioglu B, et al. Effect of preoperative oral use of erythromycin and nizatidine on gastric pH and volume. *Anaesth Intensive Care*. 2002;30:428–432. [PubMed: 12180579]

13. Gouda BB, Lydon AM, Badhe A, Shorten GD. A comparison of the effects of ranitidine and omeprazole on volume and pH of gastric contents in elective surgical patients. *Eur J Anaesthesiol.* 2004;21:260–264. doi:10.1017/S0265021504004028. [PubMed: 15109187]
14. Atanassoff PG, Brull SJ, Weiss BM, Landefeld K, Alon E, Rohling R. The time course of gastric pH changes induced by omeprazole and ranitidine: a 24-hour dose-response study. *Anesth Analg.* 1995;80:975–979. doi:10.1097/00000539-199505000-00021. [PubMed: 7726442]
15. Stuart JC, Kan AF, Rowbottom SJ, Yau G, Gin T. Acid aspiration prophylaxis for emergency Caesarean section. *Anaesthesia.* 1996;51:415–421. doi:10.1111/j.1365-2044.1996.tb07782.x. [PubMed: 8694150]
16. Tripathi A, Somwanshi M, Singh B, Bajaj P. A comparison of intravenous ranitidine and omeprazole on gastric volume and pH in women undergoing emergency caesarean section. *Can J Anaesth.* 1995;42:797–800. [PubMed: 7497561]
17. Nishina K, Mikawa K, Takao Y, Shiga M, Maekawa N, Obara H. A comparison of rabeprazole, lansoprazole, and ranitidine for improving preoperative gastric fluid property in adults undergoing elective surgery. *Anesth Analg.* 2000;90:717–721. doi:10.1097/00000539-200003000-00038. [PubMed: 10702463]
18. Cruickshank RH, Morrison DA, Bamber PA, Nimmo WS. Effect of i.v. omeprazole on the pH and volume of gastric contents before surgery. *Br J Anaesth.* 1989;63:536–540. doi:10.1093/bja/63.5.536. [PubMed: 2605070]
19. Uesugi T, Mikawa K, Nishina K, Morikawa O, Takao Y, Obara H. The efficacy of lafutidine in improving preoperative gastric fluid property: a comparison with ranitidine and rabeprazole. *Anesth Analg.* 2002;95:144–147. doi:10.1097/00000539-200207000-00025. [PubMed: 12088958]
20. Yamanaka Y, Mammoto T, Kita T, Kishi Y. A study of 13 patients with gastric tube in place after esophageal resection: use of omeprazole to decrease gastric acidity and volume. *J Clin Anesth.* 2001;13:370–373. doi:10.1016/S0952-8180(01)00289-6. [PubMed: 11498319]
21. Lin CJ, Huang CL, Hsu HW, Chen TL. Prophylaxis against acid aspiration in regional anesthesia for elective cesarean section: a comparison between oral single-dose ranitidine, famotidine and omeprazole assessed with fiberoptic gastric aspiration. *Acta Anaesthesiol Sin.* 1996;34:179–184. [PubMed: 9084544]
22. Levack ID, Bowie RA, Braid DP, et al. Comparison of the effect of two dose schedules of oral omeprazole with oral ranitidine on gastric aspirate pH and volume in patients undergoing elective surgery. *Br J Anaesth.* 1996;76:567–569. [PubMed: 8652333]
23. Hett DA, Scott RC, Risdall JE. Lansoprazole in the prophylaxis of acid aspiration during elective surgery. *Br J Anaesth.* 1995;74:614–615. doi:10.1093/bja/74.5.614. [PubMed: 7772441]
24. Boulay K, Blanloeil Y, Bourveau M, Geay G, Malinovsky JM. Effects of oral ranitidine, famotidine and omeprazole on gastric volume and pH at induction and recovery from general anaesthesia. *Br J Anaesth.* 1994;73:475–478. doi:10.1093/bja/73.4.475. [PubMed: 7999487]
25. Memis D, Turan A, Karamanlioglu B, Saral P, Ture M, Pamukcu Z. The effect of intravenous pantoprazole and ranitidine for improving preoperative gastric fluid properties in adults undergoing elective surgery. *Anesth Analg.* 2003;97:1360–1363. [PubMed: 14570652]
26. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: a report by the American Society of Anesthesiologist Task Force on Preoperative Fasting. *Anesthesiology.* 1999;90:896–905. doi:10.1097/00000542-199903000-00034. [PubMed: 10078693]
27. Nishina K, Mikawa K, Maekawa N, Takao Y, Shiga M, Obara H. A comparison of lansoprazole, omeprazole, and ranitidine for reducing preoperative gastric secretion in adult patients undergoing elective surgery. *Anesth Analg.* 1996;82:832–836. doi: 10.1097/00000539-199604000-00027. [PubMed: 8615506]

Fig. 1.

Flow diagram of the treated and modified intent-to-treat populations. Patients excluded from the modified intent-to-treat population had a baseline pH of >3 in all predose aspirates

Fig. 2. Median hourly gastric volume (a), acid output (b), and pH (c) at baseline (hour 0) and following administration of 40 mg intravenous pantoprazole every 12 h, 40 mg every 24 h, and 80 mg every 12 h. Modified intent-to-treat population

Fig. 3.

Median gastric volume (**a**) and gastric acid output (**b**) at baseline and for the first 12 h after administration of a 40 or 80 mg dose of intravenous pantoprazole. Modified intent-to-treat population. All comparisons with baseline for both volume and acid output were statistically significant ($P < 0.05$) except for the 1-h time point in the 80 mg group by gastric volume measure

Fig. 4. Median gastric acid output at baseline and during the first 12 h after administration of a 40 or 80 mg dose of intravenous pantoprazole as a 2- or 15-min infusion. Modified intent-to-treat population

Fig. 5.

The percentage of patients with at least one gastric aspirate who met the criteria for risk of aspiration pneumonia by dose at baseline and during the first 3 h following drug administration, treated population: volume >25 ml/h, pH < 2.5, and volume >25 ml/h or pH < 2.5. Modified intent-to-treat population

Table 1

Demographic and other baseline characteristics, treated population

	Pantoprazole						Total (%) (<i>n</i> = 26)
	40 mg			80 mg			
	q12h 15 min (<i>n</i> = 3)	q12h 2 min (<i>n</i> = 4)	q24h 15 min (<i>n</i> = 4)	q24h 2 min (<i>n</i> = 6)	q12h 15 min (<i>n</i> = 5)	q12h 2 min (<i>n</i> = 4)	
Mean age, years	56.0	61.3	41.5	49.8	50.6	57.8	52.4
Range							25–81
Sex, <i>n</i>							
Male	2	1	3	4	4	3	17 (65.4%)
Female	1	3	1	2	1	1	9 (34.6%)
Race, <i>n</i>							
White	2	2	4	5	4	4	21 (80.8%)
Black		1		1	1		3 (11.5%)
Hispanic	1	1					2 (7.7%)
Mean weight, kg	78.1	68.6	100.4	76.0	89.0	117.2	87.7
Range							44.2–207
Mean height, cm	178.7	161.8	175.5	170.5	174.6	177.8	172.8
Range							154–194
<i>H. pylori</i> positive, <i>n</i>	1	2	1	2	2	1	9 (34.6%)