

The Effect of Intravenous Pantoprazole and Ranitidine for Improving Preoperative Gastric Fluid Properties in Adults Undergoing Elective Surgery

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We studied pantoprazole, a new potent and fast-acting proton pump inhibitor. Its effects on preoperative gastric fluid volume and pH have not yet been determined. In this randomized, controlled trial, we examined the effects of preoperative IV pantoprazole or ranitidine on gastric pH and volume. Ninety patients (ASA status I and II, scheduled for elective surgery) were studied. One hour before surgery, patients in Group I ($n = 30$) were given IV saline 5 mL, those in Group II ($n = 30$) were given 40 mg of pantoprazole IV, and those in Group III ($n = 30$) were given 50 mg of ranitidine IV. A nasogastric tube was inserted immediately after anesthesia induction. Gastric contents were aspirated, and volume and pH were recorded. The pH values determined in Group I were 3.73 ± 0.82 ; in Group II, they were 5.30 ± 1.84 ; and in Group III, they were 4.80 ± 1.40 . There was no statistical difference between

Groups 2 and 3, but there was a significant difference between Group I and Groups 2 and 3 ($P < 0.0005$). The volume of the gastric contents was 28.67 ± 10.98 mL in Group I, 15.20 ± 15.52 mL in Group II, and 7.77 ± 11.17 mL in Group III. There was no statistical difference between Groups 2 and 3, but there was a statistically significant difference between Group I and Groups 2 and 3 ($P < 0.0005$). The proportion of patients considered "at risk" of significant lung injury should aspiration occur was 20% of Group I, 10% of Group II, and 3.3% of Group III. When statistically evaluated, there was no difference among groups. We concluded that the administration of IV pantoprazole and ranitidine 1 h before surgery is effective in reducing gastric pH and volume.

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Many drugs, including histamine-2 (H_2) receptor antagonists, proton pump inhibitors such as omeprazole, and antacids, have been used in an attempt to eliminate the risk of pulmonary aspiration by decreasing the acidity and volume of the gastric fluid (1–3). H_2 receptor antagonists inhibit secretion of gastric acid, decreasing both the pH and volume of gastric contents (3).

Proton pump inhibitors are the most effective anti-secretory drugs available for controlling gastric acid acidity and volume. They are the drugs of choice in the treatment of moderate to severe gastroesophageal reflux disease, hypersecretory disorders, and peptic ulcers (4). Recently, IV pantoprazole, a new potent

and fast-acting proton pump inhibitor, has been available in several countries. IV pantoprazole has been available in Canada since August 1999 (5). No reports concerning the effect of IV pantoprazole on preoperative gastric fluid volume and pH have been published. Our aim was to determine whether IV pantoprazole can decrease gastric acid secretion and volume during the induction of anesthesia. In our study of patients scheduled for elective surgery, we aimed to compare the effects of IV pantoprazole, IV ranitidine, or placebo given 1 h before operation on gastric acidity and volume.

Methods

After we obtained approval from the Ethics Committee and obtained informed, written consent, the study was conducted on 90 ASA status I–II patients scheduled for elective surgery. Patients with gastrointestinal diseases and those receiving medication that may have altered gastric motility were excluded from the study.

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The study design was randomized and double-blinded, with patients allocated according to a computer-generated randomization. The patients were randomized to 3 groups of 30 patients each. One hour minutes before the operation, saline 5 mL IV was given to Group I ($n = 30$), 40 mg of pantoprazole (Pantpas IV; Altana Pharma AG, Germany) IV was given to Group II ($n = 30$), and 50 mg of ranitidine (Ranitab; Deva, Turkey) IV was given to Group III ($n = 30$). Evaluation was performed by an anesthesia assistant who did not know the contents of the IV.

All of the patients were preoperatively fasted for 6 h for solid food and 4 h for liquid, and no premedication was given. Anesthetic induction was performed with propofol 2 mg/kg IV, and tracheal intubation was facilitated with atracurium 0.5 mg/kg IV. The lungs were ventilated, taking care to avoid inflation of the stomach. Anesthesia was maintained with 50% oxygen/N₂O and 1%–1.5% isoflurane. Muscle relaxation was maintained with 0.2 mg/kg atracurium IV monitored by relaxometry. All inductions were uneventful, and no patients had coughing, laryngospasm, or vomiting during the induction.

After tracheal intubation, an anesthesiologist who did not know which drug was given to the patient inserted a nasogastric tube into the stomach. Placement of the nasogastric tube within the stomach was verified by auscultation over the epigastrium during the introduction of 10 mL of air. Gastric fluid samples were obtained by gentle aspiration with a 50-mL syringe by an investigator who was unaware of the patient's preanesthetic medication. Aspirations were attempted with the patient held in supine, reverse Trendelenburg, and both lateral positions to maximize gastric emptying. At any position, pressure was applied over the epigastrium, and gastric contents were aspirated intermittently during removal of the nasogastric tube. The volume of gastric contents was measured with a syringe. The pH of the gastric contents was measured. Patients with gastric contents pH ≤ 2.5 and volume ≥ 25 mL were specified as at risk of injury in case of aspiration and were thus recorded. After aspiration of gastric contents, fentanyl 1 μ g/kg IV was given to all patients. The patients were monitored in the recovery room and then were transferred to the ward. In the ward, for 24 h, the patients were kept under the surveillance of an anesthesia specialist, who did not know which drug was given to the patient, for side effects such as nausea, vomiting, and gastric disease.

Statistical evaluation was performed by the Minitab (WCP1331.00197; Minitab, Inc., State College, PA) program. The age, weight, sex, gastric fluid pH, volume, and side effects were recorded for each patient. Comparisons of data among groups were made by using one-way analyses of variance and Tukey's test of multiple comparisons for parametric data and the χ^2 test

to establish the acid aspiration syndrome risk and side effects. $P < 0.05$ was accepted as statistically significant. Power analysis revealed that the sample size ($n = 30$ in each group) of the study was sufficient to detect medium differences ($[\text{mean } 1 - \text{mean } 2]/\text{SD} = 0.55\text{--}0.75$) in variables (pH and volume) at a significance level of 0.05 with a power of 0.65–0.85 (6,7).

Results

There were no significant demographic differences among the groups ($P > 0.05$) (Table 1). The pH values determined in Group I were 3.73 ± 0.82 , in Group II were 5.30 ± 1.84 , and in Group III were 4.80 ± 1.40 . There was no statistical difference between Groups 2 and 3, but there was a significant difference between Group I and Groups 2 and 3 ($P < 0.0005$). The volume of gastric contents was 28.67 ± 10.98 mL in Group I, 15.20 ± 15.52 mL in Group II, and 7.77 ± 11.17 mL in Group III. Again, there was no difference between Groups 2 and 3, but there was a significant difference between Group I and Groups 2 and 3 ($P < 0.0005$) (Table 2).

The proportion of patients classified as "higher risk" in case of aspiration was 20% in Group I, 10% in Group II, and 3.3% in Group III (Table 3). Although the acid-aspiration risk in Group I was somewhat higher than Groups II and III, the difference was not statistically significant. There was no significant difference in nausea or vomiting (5, 6, and 7 patients in Groups I, II, and III, respectively), and no other adverse effects were encountered.

Discussion

Pantoprazole, developed in Germany, is the third of the proton pump inhibitors after omeprazole and lansoprazole (8). IV pantoprazole has been available in Canada since August 1999 (5). It is a potent proton pump inhibitor (H, K-adenosine triphosphatase) for activity and acid output. The drug is activated in the acidic lumen of the gastric parietal cells. Pantoprazole inhibits the acid secretion provoked by histamine, pentagastrin, or dibutyryl cyclic adenosine monophosphate. Pantoprazole shows greater *in vitro* antimicrobial activity against *Helicobacter pylori* (8). The drug does not alter endocrine function (testosterone, cortisol, insulin, glucagon, and thyroid function). Pantoprazole provides earlier healing and superior pain relief in peptic ulcer and gastroesophageal reflux disease compared with omeprazole or H₂ receptor antagonists (8,9).

As with many other studies concerning gastric fluid properties (2,3,7,10), we used blind aspiration to measure the volume of gastric contents. This technique may incompletely empty the stomach and, therefore,

Table 1. Demographic Data of Patients and Type of Surgery (Mean ± SD)

Variable	Group 1 (n = 30)	Group 2 (n = 30)	Group 3 (n = 30)
Age (yr)	45 ± 22	48 ± 22	51 ± 17
Weight (kg)	78 ± 12	75 ± 14	81 ± 14
Sex (M/F)	12/8	11/9	11/9
Surgery type (n)	Hysterectomy (10) Arthroscopy (8) Lumbar discectomy (4) Nerve repair (4) Cystoscopy (2) Mammoplasty (2)	Hysterectomy (9) Arthroscopy (6) Varicose vein (6) Cystoscopy (2) Lumbar discectomy (4) Inguinal hernia (3)	Hysterectomy (13) Arthroscopy (4) Varicose vein (4) Cystoscopy (2) Lumbar discectomy (4) Inguinal hernia (3)

There were no statistically significant differences among the groups.

Table 2. Gastric Contents: pH and Volume (Mean ± SD)

Variable	Group 1 (n = 30)	Group 2 (n = 30)	Group 3 (n = 30)
pH of gastric contents ^a	3.73 ± 0.82	5.30 ± 1.84	4.80 ± 1.40
Volume of gastric contents (mL) ^b	28.67 ± 10.98	15.20 ± 15.52	7.77 ± 11.17

^a There was no statistical difference between Groups 2 and 3, but there was a statistically significant difference between Group 1 and Groups 2 and 3 (*P* < 0.0005).

^b There was no statistical difference between Groups 2 and 3, but there was a statistically significant difference between Group 1 and Groups 2 and 3 (*P* < 0.0005).

Table 3. Patients at Increased Risk of Lung Injury

Variable	Group 1 (n = 30)		Group 2 (n = 30)		Group 3 (n = 30)	
	n	%	n	%	n	%
Patients with gastric content pH ≤2.5	10	33.3	5	16.6	3	10
Patients with gastric content volume ≥25 mL	7	23.3	6	20	3	10
Patients with gastric content pH ≤2.5 and volume ≥25 mL	6	20	3	10	1	3.3

There were no statistically significant differences among the groups.

underestimate gastric fluid volume. The alternative methods include gastric aspiration by using a visually guided gastroscope and the dye-dilution technique (11). Estimated gastric volume by the dye-dilution method has been shown to be similar to aspirated volume by blind aspiration despite being complicated and time consuming (12).

Pantoprazole has a low affinity for the cytochrome P450 system of the liver. In studies conducted to investigate interactions between pantoprazole and other drugs, it has been shown that no interactions occur between pantoprazole and antacids, antipyrine, caffeine, carbamazepine, diazepam, diclofenac, nifedipine, warfarin, phenytoin, and so on (13). Ranitidine also has a low affinity for the cytochrome P450 system (14). A variety of adverse reactions have been ascribed to ranitidine, reflecting, in part, the very large number of patients who have been treated with this drug (14). The incidence of reactions is small, and the reactions are generally minor. The infrequent incidence is attributable in part to the limited function of H₂ receptors in organs other than the stomach and to the poor penetration of these drugs across the normal blood-brain

barrier (14). In our study there was no significant difference in nausea and vomiting, and no other adverse side effects were encountered. IV pantoprazole and ranitidine can be used in situations in which oral treatment is not feasible (e.g., unconscious patients or those with a full stomach). Thus, the advantages and safety of IV pantoprazole and ranitidine have encouraged us to use these drugs before surgery.

Recent guidelines by the American Society of Anesthesiologists Task Force on Preoperative Fasting do not recommend routine preoperative use of gastric acid secretion blockers (H₂-receptor antagonists or proton pump inhibitors) or combinations of these and other drugs (antacids and so on) to decrease the risks of pulmonary aspiration in patients who have no apparent increased risk for pulmonary aspiration because there is not sufficient published evidence to evaluate whether reduced gastric acid secretion is associated with decreased morbidity and mortality (15). We used ASA physical status I and II patients to ensure a safe approach to the initial evaluation of pantoprazole's and ranitidine's effects. Also, according to our results, IV pantoprazole and ranitidine can

be used safely before elective surgery, as well as in uncooperative oral intake-restricted patients.

We conclude that IV pantoprazole and ranitidine administered one hour before surgery may be useful in decreasing the volume and increasing the pH of gastric content and thus reduce the proportion of patients at risk of significant lung injury should aspiration occur.

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