Original Article

Comparison of the effect of a single dose of erythromycin with pantoprazole on gastric content volume and acidity in elective general surgery patients

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Abstract

Introduction: Pulmonary aspiration of gastric contents remains one of the most feared complications of anesthesia. A gastric pH of 2.5 or less and a volume of 25 ml (0.4 ml/kg body weight) or more in average adult patients are considered critical factors for the development of pulmonary damage in adults.

Materials and Methods: This study compared the efficacy of a single oral dose of erythromycin (a macrolide antibiotic) with oral pantoprazole (a proton pump inhibitor) on pre-operative gastric fluid volume and pH in a prospective, randomized, double-blind controlled fashion in 80 adult patients (of ASA physical status I and II) planned for elective surgery under general anesthesia. Patients were divided into two groups of 40 patients each. The pantoprazole group (Group I) received oral pantoprazole 40 mg and the erythromycin group (Group II) received oral erythromycin 250 mg at least 1 h prior to the induction of anesthesia. After tracheal intubation, gastric fluid was aspirated via a Salem Sump tube and its volume and pH were measured.

Results: Although both erythromycin and pantoprazole decreased the gastric fluid volume to a similar extent, the decrease in gastric fluid acidity by pantoprazole was significantly greater than that by erythromycin. The proportion of patients at risk of pulmonary aspiration according to traditional criteria, i.e. pH ≤2.5 and volume ≥25ml, was lower in the pantoprazole group.

Conclusion: Administration of pantoprazole was found to be more useful than a sub-therapeutic dose of erythromycin in decreasing both volume and acidity of gastric content.

Key words: Erythromycin, gastric fluid volume and pH, pulmonary aspiration, pantoprazole

Introduction

Pulmonary aspiration of gastric contents still remains one of the most feared complications of anesthesia even more than 100 years after the institutionalization of general anesthesia.[1] Acid aspiration syndrome (Mendelson syndrome) has a high morbidity and mortality although, fortunately, the incidence of pulmonary aspiration under general anesthesia has steadily declined in the past few decades.[2] Mendelson syndrome produces an asthma-like reaction consisting of dyspnea, cyanosis, tachycardia and expiratory wheeze due to a peribronchiolar exudative and congestive reaction. Mendelson had clearly demonstrated in his animal experiments that acidity of the aspirate is the major etiologic factor in aspiration pneumonitis and prior neutralization of the acidic contents of the aspirate reduces the incidence of pulmonary complications.[3]

A gastric pH of 2.5 or less and a volume of 25 ml (0.4 ml/kg body weight) or more in an average adult are considered critical factors for the development of pulmonary damage in adults.[4] As laryngeal protective reflexes are impaired during general anesthesia and muscle relaxation, the regurgitated acidic contents may eventually reach the lungs and result in pulmonary aspiration and its consequent effects.[5]

Over the years, a variety of measures have been taken to guard against regurgitation or aspiration and minimize the effect of gastric contents on the lungs. These include pre-operative fasting, pre-anesthetic emptying of the stomach with the nasogastric tube,

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Sellick's maneuver and use of apomorphine, prokinetic agents, particulate/non-particulate antacids, H_2 receptor antagonists and/or proton pump inhibitors (PPIs).[6]

PPIs have demonstrated gastric acid suppression superior to H_2 receptor blockers as they act on the final step in the stimulatory process for acid secretion.[7] PPIs form a covalent (irreversible) bond at two sites of H^+K^+-ATPase (proton pump) on the secretory surface of gastric parietal cells, resulting in anti-secretory effects for 24-72 h, and have minimal side-effects or drug interactions.[8]

Several studies have shown that a sub-therapeutic dose of erythromycin (a macrolide antibiotic) accelerates gastric emptying of both solids and liquids in healthy volunteers[9] as well as in patients with delayed gastric emptying due to pathological reasons.[9,10] Erythromycin in a sub-therapeutic dose (200 mg), given as an oral pre-medication, has recently been shown to alter the residual gastric volume and its acidity in fasted patients scheduled for elective surgery.[11]

Survey of the literature reveals a lack of scientific studies evaluating the clinical efficacy of erythromycin in acid aspiration syndrome against pantoprazole in patients undergoing elective surgery under general anesthesia. This study was planned to compare the efficacy of a single oral dose of erythromycin with pantoprazole on the pre-operative gastric fluid volume and pH in patients planned for elective surgery under general anesthesia.

Materials and Methods

After the approval of the Hospital Ethics Committee and written informed consent of patients, this study was conducted with the objective of evaluating and comparing the effect of pre-operative oral erythromycin and pantoprazole on gastric volume and pH in patients undergoing elective surgery under general anesthesia. A total of 80 patients of either sex, in the age group of 20-60 years and of physical status ASA I and II, were included in the study. Based on a previous study,[12] the mean difference and pooled standard deviation was calculated and the sample size was determined (40 in each of the two groups), with power of the study being 80% and confidence interval being 99%. The study was conducted in a double-blind, randomized, controlled fashion. Numbered containers were used to implement the random allocation sequence. Patients with gastric acid secretory or motility disorder, taking drugs known to influence gastric acidity, volume or motility, renal or hepatic disease, burn patients, known diabetics, patients with a history of prior gastrointestinal surgery, pregnant females and obese adults, with weight 25% more than the ideal, were excluded.

All basic investigations required for a particular surgery were undertaken. Patients were kept fasting overnight and pre-medicated with alprazolam 0.25 mg a night before surgery and 2 h before the scheduled time of surgery. Patients were grouped randomly according to block randomization into two groups of 40 each. The pantoprazole group (Group I) received oral pantoprazole 40 mg and the erythromycin group (Group II) received oral erythromycin 250 mg with 10 ml of water at least 1 h prior to the induction of anesthesia. A standard technique for the conduct of anesthesia was used in all patients. After endotracheal intubation, an 18 Fr Salem Sump tube was passed into the stomach and correct positioning was confirmed by aspiration of typical gastric juice or auscultation of injected air into the stomach. With the patient in supine, right lateral and anti-Trendelenburg positions, gastric fluid was aspirated into a 50 ml syringe by the investigator who was unaware of the group drug. The volume of gastric juice was measured directly from the 50 ml syringe and pH measurement was performed immediately after collecting the contents in a beaker with a digital electronic pH meter, with a range of 0-14 pH and accuracy of ±0.01 pH [Digital pH meter, Model no. 131 E; M.S. Electronics (INDIA) Pvt. Ltd, Panchkula, India]. The volume of gastric juice and pH was recorded according to the group under study. The results obtained were analyzed statistically using the "unpaired *t*-test" for comparison between groups after assessing the data for significance by the ANOVA test. The Chi square test was used to compare the proportion of patients at risk in various groups. $P < 0.05$ was taken as statistically significant.

Results

Of the 88 patients assessed for eligibility, five patients did not meet the inclusion criteria and three patients refused to participate. The remaining 80 patients randomly received either of the drugs and were evaluated for gastric fluid pH and volume. Both the groups were comparable with regard to age, gender, height, weight, body mass index, duration of surgery, fasting interval and interval between drug administration and anesthesia induction [Table 1].

Gastric fluid volume and pH

The difference in volume of gastric fluid was statistically insignificant when the two groups were compared ($P > 0.05$), whereas the difference in gastric fluid pH between the two groups was statistically highly significant ($P < 0.01$) [Table 2].

Patients at increased risk of lung injury

Of the 40 patients in each group, a statistically significant number of patients ($P < 0.01$) had gastric content pH

Table 1: Demographics

	Group I (pantoprazole)	Group II (erythromycin)
Age (years)	40.4 ± 9.39	38.9 ± 11.86
Sex (M/F)	7/33	10/30
Weight (kg)	60.27 ± 10.15	58.65 ± 12.23
Height (m)	1.60 ± 4.57	1.59 ± 6.67
BMI (kg/m^2)	23.40 ± 3.9	23.01 ± 4.17
Duration of surgery (min)	90.20 ± 25.10	95.10 ± 20.25
Hours of fasting	8.61 ± 0.65	8.5 ± 0.66
Drug adminstration: anesthesia induction interval (min)	66.62 ± 6.54	68.50 ± 10.75

Values are expressed as mean ± SD

Table 2: Gastric fluid volume, pH and patients at increased risk of lung injury

	Group I (pantoprazole) (n = 40)	Group II (erythromycin) (n = 40)
Volume (ml)	12.30 ± 11.60 (8.58–16.01)*	14.76 ± 8.805 (11.94–17.57)*
Volume (ml/kg)	0.202 ± 0.194 (0.14–0.26)*	0.255 ± 0.162 (0.20–0.30)*
pH	4.93 ± 2.03 (4.28–5.58)*	3.48 ± 1.85 (2.89–4.07)*
No. of patients with gastric vol ≥ 25 ml	5/40 (12.5%)	8/40 (20%)
No. of patients with gastric pH ≤ 2.5	5/40 (12.5%)	17/40 (42.5%)
No. of patients with gastric vol ≥ 25 ml and pH ≤ 2.5	1/40 (2.5%)	4/40 (10%)

*Values are expressed as mean ± SD. *95% confidence interval for mean*

≤2.5 in Group II as compared with Group I. Although no significant difference ($P > 0.05$) was found between the two groups with regard to the number of patients with gastric aspirate volume ≥25 ml, significantly more number of patients ($P < 0.01$) in Group II had both gastric aspirate volume ≥25 ml as well as pH ≤ 2.5 [Table 2].

Adverse effects

No patient in any of the groups had any adverse effects like nausea, vomiting, skin rash, headache and dizziness.

Discussion

The level of damage to the lungs as a result of aspiration of gastric content depends on the pH and volume of the aspirated substance. A pH of ≤2.5 and volume ≥25 ml of aspirated gastric contents have been suggested as critical values (Roberts-Shirley criteria) for the development of acid aspiration syndrome.[4] Low-volume pulmonary aspirates (0.3 ml/kg) with extremely low pH (1.0) result in high mortality. Seventeen percent to 64% of the patients who have even been fasting are said to be at risk before elective surgery.[13]

Administration of drugs to alter the gastric contents favorably improve safety in anesthesia practice. The ideal method of prophylaxis should aim at maintaining a minimal intragastric volume with a high pH. Many pharmacological attempts, including the use of antacids, prokinetics, H2 blockers and PPIs, have been made to eliminate the risk of pulmonary aspiration by increasing the pH and decreasing the volume of gastric fluid, but no ideal regimen has yet been defined. Antacids (particulate and non-particulate) increase the volume of gastric fluid[4] and can cause pulmonary injury if aspirated.[14] H_2 receptor antagonists are rarely used because of their reported association with sinus bradycardia, atrioventricular block, hepatotoxicity and neuropsychiatry complications.[15,16]

PPIs are considered superior and well known to decrease gastric volume and acidity.[7,8,17,18] As H^+K^+ATPase represents the final step in the secretory process, inhibition of this enzyme suppresses gastric acid secretion irrespective of the primary stimulus. Although all the PPIs are rapidly activated under strongly acidic conditions (pH <3.0), pantoprazole is chemically more stable than omeprazole, lansoprazole and rabeprazole.[19]

Several recent studies have also shown that sub-therapeutic doses of erythromycin, a macrolide antibiotic, accelerates gastric emptying of both solids and liquids.[20-22] Asai *et al.* demonstrated that erythromycin, in sub-therapeutic doses, significantly reduced the gastric content volume and acidity when given 1 h prior to anesthesia induction.[11] At a sub-therapeutic dosage, it causes intermittent gastric contractions that spread to the small intestine, but in therapeutic doses of 500-1000 mg, it causes strong gastric contractions.[23,24] The effect of reducing gastric content volume by erythromycin may be explained by this mechanism. Although the mechanism by which erythromycin reduces gastric acidity is not fully known, it might be doing so by directly affecting the motilin receptors.[23-25] A recent study by Omar *et al.* showed that a sub-antibiotic dose of erythromycin was an inexpensive prokinetic with a promising post-operative profile.[20] We studied 80 adult ASA class I and II patients with no additional risks of pulmonary aspiration. At least 60 min was allowed to elapse between drug administration and collection of the gastric fluid sample because erythromycin is known to alter gastric fluid acidity when given at least 1 h prior but not if given 3 h prior.[11]

A Salem Sump tube was used to aspirate the gastric contents as suction applied to a single-lumen nasogastric tube (e.g., Ryle's tube) may pull the gastric mucosa into the drainage eyes, preventing further aspiration. The double-lumen Salem Sump tube avoids this by allowing air flow through the vent lumen while gastric fluid is being aspirated through the main

lumen.[26] Functional division of stomach into antral and fundal sacs may affect the efficiency of blind aspiration. To minimize this error, we positioned our patients in supine, anti-Trendelenburg and in left lateral positions as described by Maughan *et al*.[27]

In our study, both pantoprazole and a sub-therapeutic dosage of erythromycin, when given at least 1 h prior to elective surgery, were found to decrease the gastric content volume and acidity. Although the differences in the decrease of gastric content volume by pantoprazole and erythromycin were statistically not significant, the difference in increase of gastric fluid pH between the two groups was statistically highly significant, with pantoprazole decreasing the gastric fluid acidity to a greater extent than erythromycin. Although the number of patients having gastric fluid volume ≥25 ml were higher in the erythromycin group as compared with the pantoprazole group, this difference was not statistically significant. Significantly larger number of patients receiving erythromycin were found to have gastric fluid pH ≤2.5 as compared with those receiving pantoprazole, making the patients receiving erythromycin more prone to the risk of lung injury following acid aspiration.

To conclude, pre-operative administration of pantoprazole is more useful than a sub-therapeutic dose of erythromycin in decreasing both the volume and the acidity of the gastric content and thus reducing the proportion of patients at risk of significant lung injury should aspiration occur.

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