Gastric pH in patients premedicated with Esomeprazole or Famotidine undergoing routine surgery under general anaesthesia

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Abstract

Background: Stress and anxiety in patients planned for surgery under anaesthesia may change pH of gastric secretion. Premedication of surgical patients with pH altering drugs may modify the pH favourably. With the advent of newer agents, premedication has been carried out with different agents. Most of the time choice of drug is made by the perioperative physician on his/her own.

Objective: To study gastric pH in patients premedicated either with Esomeprazole or Famotidine.

Methods: This is a randomized controlled double blind prospective study conducted in 150 patients of American Society of Anesthesiologists grade I and II posted for elective surgery under general anaesthesia. The patients enrolled in the study were randomly assigned to three groups having 50 patients in each. Group I (control group) did not receive any pH altering drug, Group II (Famotidine Group) received 40 mg of Famotidine and Group III (Esomeprazole Group) received 40 mg of Esomeprazole the night before surgery. The observer was totally blind about the groups or drugs given to the patients. On the day of surgery, after induction of anaesthesia gastric juice was obtained via nasogastric tube and was checked for pH using pH indicator paper.

Results: The pH raised by Esomeprazole was statistically significant ($p<0.001$) when compared to that of control group or Famotidine group. The mean pH value in control group was less than 2.5 whereas the pH value was higher than 2.5 in patients premedicated with either Famotidine or Esomeprazole.

Conclusions: Gastric pH is raised by Famotidine or Esomeprazole premedication prior to routine surgery, Esomeprazole being superior to Famotidine, $p<0.001$. Patients (84%) not premedicated with either of the drugs had pH less than 2.5.

Key words: Anaesthesia, Esomeprazole, Famotidine, Gastric pH, Premedication.

INTRODUCTION

General anaesthesia predisposes a patient to regurgitation and aspiration of gastric substances into otherwise healthy lungs leading to fatal acid aspiration syndrome. Historically, the syndrome most commonly described as aspiration pneumonitis or Mendelson's syndrome, was reported in 1946, in patients who aspirated while receiving general anaesthesia during obstetrical procedures[1]. Every practicing anaesthesiologist thus has a key concern to this preventable devastating clinical condition which causes progressive lung damage due to the acidic solution. This morbidity demands intensive and prolonged pulmonary support. Acidity and volume of the gastric regurgitate have been considered the two important factors for causing aspiration pneumonia syndrome in humans. It is generally agreed that pH value of gastric regurgitate less than 2.5 and a volume of more than 25 ml is critical in producing aspiration pneumonia syndrome[2-5]. Normal pH of gastric juice is two to three[6]. Without any attempts to decrease the acidity of gastric secretion, there is always a risk of soiling the pulmonary system should aspiration occur perioperatively. Different pharmacological agents have been available in clinical use for prevention of acid peptic diseases. Newer agents are progressively evolving either from H_2 receptor antagonist group or from proton pump inhibitor (PPI) groups.

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The choice of these agents as a premedication by anaesthesiologists varies from person to person. Recently, Esomeprazole, a new PPI has become available for clinical use. It is chemically more stable than other available PPIs and has a more effective control of acid secretion[7,8]. Evolution of newer drugs led to almost abstinence of easily available cheaper agents like Famotidine from its extensive clinical use before any evidence based clinical research.

Data of these drugs on pH of gastric secretion when used as a premedication in surgical patients may help to choose the drugs and warn the perioperative clinicians of not conducting prophylaxis prior to anaesthesia and surgery.

Thus we conducted a double blind randomised controlled study to evaluate the efficacy of oral Famotidine and Esomeprazole in increasing the gastric pH in patients undergoing routine surgery under general anaesthesia.

This study was done to study gastric pH in patients premedicated with Esomeprazole or Famotidine and to find out the pH in control group.

METHODS

This is a randomised controlled double blind prospective study conducted in 150 American Society of Anesthesiologists (ASA) grade I and II patients posted for elective surgery under general anaesthesia from 2nd March 2012 to 5th August 2012 in Kathmandu Medical College Teaching Hospital. The study was initiated following approval of the protocol from institutional review board and ethical committee.

All the patients were fasted overnight and premedicated with tablet Lorazepam one mg and Metoclopramide 10 mg the night before surgery. All the patients enrolled in the study were randomly assigned by lottery method to three groups with 50 patients in each. Group sizes of 50 were determined by the power study based on standard deviation data from previously published reports[9,10].

Group I (Control group) received no pH altering drug, Group II (Famotidine Group) received 40 mg of Famotidine and Group III (Esomeprazole Group) received 40 mg of Esomeprazole the night before surgery. The observer was totally blind about the groups or drugs given to the patients.

Intravenous (IV) access was secured with 18 G cannula and cardiovascular and respiratory monitors were applied to the patients on arrival to the operation room. General anaesthesia was induced with injection Propofol (2 mg/kg). Analgesia was achieved with injection Fentanyl 2 mcg/kg Injection Rocuronium 1 mg/kg IV was used for muscle relaxation. Lungs were ventilated manually with mixture of oxygen, air and Isoflurane. After complete relaxation, orotracheal intubation was accomplished with an endotracheal tube of appropriate size. Respiration was then taken under control by intermittent positive pressure ventilation adjusted as per the physiology. Maintenance of general anaesthesia was continued with Isoflurane.

An 18 F orogastric tube was passed down to the stomach and its position was verified by auscultation over the epigastrium with insufflations of 10 ml of air. About 0.5 to one ml of gastric fluid obtained via orogastric tube was subjected to subsequent pH measurement using pH indicator paper. The change in colour of pH indicator paper was standardized comparing the given colour code. Surgery was then asked to proceed. At the end of the surgery the effect of muscle relaxant was antagonized with intravenous Neostigmine 0.05mg/kg and Glycopyrrolate 0.02 mg/kg. Trachea was extubated after the criteria for extubation was met.

Inclusion Criteria: All patients of ASA grade I and II with age between 18-75 years from both sexes with body weight of 35 - 80 kg undergoing elective surgery under general anaesthesia were enrolled in the study.

Exclusion Criteria: The following criteria were adopted for the patients not to be included in the study:

1. Patients suffering from gastric, duodenal acid peptic disease, pregnant and those who were under treatment with antacids, H_2-blockers or PPIs.
2. Patients with known history of allergy or idiosyncrasy to Famotidine or Esomeprazole.
3. Patients grouped as ASA physical status other than I and II and who had been planned to undergo gastric, duodenal or oesophageal interventions.
4. Patients with difficult airways not expecting to receive long acting muscle relaxant.
5. Failure of passing NG tube or obtain gastric aspirate. Obtaining yellowish bile mixed aspirate.

The demographic characteristics age, weight, sex and starvation hours and gastric pH data were recorded. Medians of parametric tests were subjected to analysis by Analysis of Variance (ANOVA) test and that of non-parametric tests between groups were compared

by Kolmogorov-Smirnov test. The level of statistical significance was set at $p<0.05$.

RESULTS

The demographic characteristics of the patients in three groups were not different (Table1).

There was a tendency of low pH in control group than in Famotidine or Esomeprazole group. The mean pH value in control group was less than 2.5 whereas the pH value was higher than 2.5 in patients premedicated with either Famotidine or Esomeprazole. Esomeprazole has been found to increase the pH of the gastric juice effectively and the pH raised by Esomeprazole was more as compared to that of control group or Famotidine group and the difference was statistically significant. Famotidine also significantly decreased the acidity of gastric secretion when compared to control group. Eighty four percentage of the patients in Control group had their gastric pH less than 2.5, whereas in Famotidine and Esomeprazole groups, the proportion was 32% and 14% respectively. Only 16% in control group had pH more than 2.5.The value increased up to 68% in Famotidine and 86% Esomeprazole groups. Famotidine 40 mg or Esomeprazole 40 mg given as a premedication in patients undergoing general anaesthesia effectively decrease gastric juice acidity to a pH more than 2.5. Esomeprazole has been found to be superior to Famotidine in this regard.

Table 1: Demographic characteristics of patients in study groups.

Parameters (Mean± SD)	Control Group (C)	Famotidine Group (F)	Esomeprazole Group (E)	p value
Age, years	38.56 ±12.88	41.56±12.88	41.48±15.83	C vs. F=0.225 F vs. E=0.914 E vs. C=0.314
Weight, kg	55.94±11.76	57.92±12.96	59.60±9.85	C vs. F=0.41 F vs. E=0.09 E vs. C=0.46
Sex, Male:Female	36:14	32:18	32:18	
Fasting duration, hours	10.34±1.75	10.48±1.63	10.18 ±1.42	C vs. F=0.68 F vs. E=0.33 E vs. C=0.61

Table2: Gastric pH in the study groups.

	Number of patients	Gastric pH	p value
Control Group (C)	50	2.15 ± 1.78	C vs. F=0.020
Famotidine Group (F)	50	4.06 ± 2.54	F vs. E=0.000
Esomeprazole Group (E)	50	5.78 ± 1.99	E vs. C=0.000

Table 3: Distribution of cases as per pH more than or less than 2.5

Study Groups	pH >2.5	pH <2.5	Total
Control	8 (16%)	42 (84%)	50
Famotidine	34 (68%)	16 (32%)	50
Esomeprazole	43 (86%)	7 (14%)	50

Table 4: Distribution of patients as per ASA* class:

	Control Group	Famotidine Group	Esomeprazole Group
ASA I	35	38	34
ASA II	15	12	16
Total	**50**	**50**	**50**

*American Society of Anaesthesiologists

Table 5: Surgical Procedures in study groups

	Control Group	Famotidine Group	Esomeprazole Group
Laparoscopic Cholecystectomy	30	28	32
Pyelolithotomy	7	2	2
MRM*	2	3	4
TAH†	8	7	5
PCNL‡	3	2	2
FESS§	0	3	5
Tonsillectomy	0	3	0
Parotidectomy	0	2	0
Total	**50**	**50**	**50**

*Modified Radical Mastoidectomy
†Total Abdominal Hysterectomy
‡Percutaneous Nephrolithotomy
§Functional Endoscopic Sinus Surgery

DISCUSSION

This study reveals that premedication with oral Famotidine 40 mg or Esomeprazole 40 mg the night before surgery in patients that fasted for mean duration of 10 hours significantly raised pH of gastric aspirate, Esomeprazole being superior to Famotidine. Patients in control group had pH less than 2.5.

The age and weight of patients in three study groups did not differ. The male to female gender distribution of the patients in the study groups was also similar.

The mean pH in control group was 2.15 which was significantly lower than in Famotidine (mean pH 4.06) and Esomeprazole group (mean pH 5.78), p<0.001. This result is consistent with the findings of the study conducted by Miner P Jr et al and Edwards SJ et al[11,12]. A single dose of intravenous Esomeprazole 40 mg administered prior to surgery raised the gastric fluid pH to the same range of 5.5 in the study by Sadawarte SM et al[13].

Wilder Smith SH et al found Esomeprazole providing faster and effective control of intragastric pH than Pantoprazole[14].

Boulay K, Blanloeil Y et al compared ranitidine, Famotidine and Omeprazole in 150 patients to determine pH at induction of general anaesthesia and discovered the median gastric pH was lower with Omeprazole compared with Ranitidine and Famotidine at intubation (5.11, 7.05 and 6.99 respectively) (P < 0.001)[9]. This study also shows that PPIs are superior to H_2 receptor blockers in decreasing gastric acidity.

Esomeprazole 20 mg given orally night prior to surgery raised the gastric pH to 4.75 in a study conducted by Hussein A et al, the mean value of pH being less than the current study which could be related with smaller dose[10]. Hussein A et al excluded the cases in case of aspiration mixed with bile to rule out possible bile contamination altering the gastric pH. We also employed the same technique excluding one case. One more case was excluded from the study because of inability to obtain the gastric fluid via orogastric tube. Two more cases were later enrolled in respective groups to make up for the loss.

Gastric juice of 0.5 to one ml was obtained immediately following induction of anaesthesia keeping in view the findings of a study by Biswas BK et al which states that duodenogastric reflux is possible once laparatomic cholecystectomy has been proceeded[15]. Our study included maximum cases of laparoscopic surgery and the pH of the gastric secretion could be changed following intraperitoneal carbon dioxide insufflations according to the study by Lee S II et al[16]. Thus in laparoscopic surgery pH of gastric juice was recorded in all cases prior to creation of pneumoperitoneum in the current study.

There are different methods of estimating gastric pH described in literatures like platin-antimony pH probe and pH indicator paper[17].

We used orogastric tubes for manual aspiration of the fluid from stomach and pH paper was utilized for the pH record. This method is cheaper than and as effective as pH meter[18].

Fasting, pain and stress of surgery are indispensible factors which might increase the gastric acidity even in healthy patients. American Society of Anesthesiologists task force guidelines on perioperative fasting do not recommend routine use of gastric acid secretion antagonists to decrease the risk of acid aspiration syndrome in healthy patients scheduled for routine surgery as well.

This study reveals that the pH is less than 2.5 in control group; putting the patients on at least one risk factor (gastric volume not studied) should aspiration occur following general anaesthesia. Moreover, this can be employed in patients with high risk factors with obvious reasons. According to the literatures, the incidence of aspiration pneumonitis contributed by general anaesthesia in surgical population is only one in 9,209[19]. There are literatures reporting this incidence to be one in 3,000 operations under general anaesthesia which accounts for 10 to 30 percent of all deaths associated with anaesthesia[20]. The data is seriously lacking and unavailable in our context.

Once the incidence encountered, the mortality rate is very high[21]. This warrants premedication even in healthy surgical population and is justifiable as regurgitation and acid aspiration in per operative period can hardly be predicted in usual anaesthetic practice.

The objective of the current study was to find out the gastric pH, not the secretory function following premedication or study of incidence of regurgitation and acid aspiration in surgical population. Obviously this study does not provide answer to how many patients were at real risk of aspiration pneumonitis or pneumonia.

After oral administration, the onset of the anti-secretory effect of Famotidine occurs within one hour; the maximum effect is dose-dependent, occurring within one to three hours. Duration of inhibition of secretion by doses of 20 and 40 mg are 10 to 12 hours[22].

After oral doses, peak plasma levels occur in one to three hours. Plasma levels after multiple doses are similar to those after single doses. Fifteen to 20% of Famotidine is bound to plasma protein. It has an elimination half-life of 2.5 to 3.5 hours and is eliminated by renal (65-70%) and metabolic (30-35%) routes[22]. Esomeprazole is the latest of the five proton pump inhibitors (Omeprazole, Lansoprazole, Pantoprazole and Rabeprazole) and single dose is effective for 24 hours extending its effect beyond the operation theatres once premedicated in surgical patients[23].

In our study, 84 % of patients had pH <2.5 in control group whereas only 14% in Esomeprazole group, showing the importance of preoperative premedication.

CONCLUSION

Gastric pH is raised by Famotidine or Esomeprazole premedication prior to routine surgery, Esomeprazole being superior to Famotidine. Patients not premedicated with either of the drugs have pH less than 2.5.

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