

ORIGINAL ARTICLE

A comparison of the effects of erythromycin and metoclopramide on gastric fluid volume and pH in patients undergoing elective caesarean section

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ABSTRACT

Objective: To compare the effects of erythromycin and metoclopramide on gastric fluid volume and pH in patients undergoing elective caesarean section.

Study Design: Randomized, controlled trial.

Place and Time Period: The study was conducted in Gynaecology Ward and Operation Theatre, Rehman Medical Institute Peshawar from July 2009 to June 2010.

Methodology: We recruited 144 patients, ASA grades I and II, scheduled to undergo elective caesarean section and divided them in two equal groups of 72 patients each by simple random sampling. Patients in group A were given tablet erythromycin 250 mg and patients in group B were given tablet metoclopramide 10 mg orally with 10ml of water one hour before surgery. Both groups were then compared in terms of gastric fluid volume and gastric pH according to Robert and Shirleys' criteria, using a cut off value of 25 ml and pH 2.5, respectively. Statistical analysis was done by applying Chi-Square test and Students' T- test.

Results: Among the patients of group A 87.5% patients had acceptable volume (25ml) and 62.5% patients had acceptable pH of gastric fluid (pH \geq 2.5). In group B patients 69.4% patients had acceptable gastric fluid volume and 19.4% patients had acceptable pH of gastric fluid.

Conclusion: Oral erythromycin reduces gastric fluid volume more effectively than metoclopramide, if given one hour before surgery. Erythromycin increases while metoclopramide has no effect on the pH of gastric fluid.

Key Words: Metoclopramide; Erythromycin; Gastric fluid volume; pH; Aspiration pneumonitis.

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INTRODUCTION

Acute aspiration pneumonitis (AP) remains one of the major causes of death related to anesthesia¹. Routine aspiration prophylaxis is not recommended but it may be carried out in some patients in whom gastric emptying is delayed. The delayed gastric emptying occurs primarily in

conditions like pregnancy, diabetes mellitus, morbid obesity, old age and hiatal hernia; thus predisposing these patients to a significant risk for pulmonary aspiration during anesthesia², and therefore necessitates prophylactic measures in this particular group of patients.

Parturients are at high risk of developing AP as they are considered to be full stomach regardless of the time of last oral intake. They have large residual volume of gastric fluid despite prolonged fasting. Most of these patients may have gastric fluid volume >25ml and pH <2.5 even after long periods of fasting³. This makes them vulnerable to regurgitation and aspiration of gastric contents during induction of general anesthesia. Attempts have been made to manipulate the volume and pH of gastric fluid prior to the conduct of anesthesia. Maneuvers include use of antacids, prokinetic drugs, H₂-receptor antagonists⁴ and nasogastric aspiration.

Metoclopramide can be used to reduce gastric fluid volume and acidity but its use is restricted mainly by its potential to produce extrapyramidal effects. Erythromycin is also an effective prokinetic agent but devoid of similar side-effects. Studies have shown that sub-therapeutic doses of erythromycin accelerate gastric emptying in more patients and better reduce acidity as compared to metoclopramide^{5,6}. The use of erythromycin for this purpose is somehow not a preferred method and instead metoclopramide is still widely used despite its side effects.

We designed this study to highlight the usefulness of erythromycin by comparing erythromycin with metoclopramide as a premedication for reducing gastric fluid volume and acidity in order to decrease the risk of aspiration pneumonitis in parturients undergoing elective caesarean section.

METHODOLOGY

This study was an interventional analytical study carried out in Gynaecology & Obstetrics ward and operating rooms, Rehman Medical Institute, Peshawar. After approval from the hospital ethical committee, a total of 144 patients, planning to undergo elective caesarean section, were selected for this study. Sample size was calculated in order to detect a difference of 20% between the two medications with 80% power and 95% significance levels. Thus, 72 subjects were required to be included in the study for each group. Patients included in the study met the following inclusion criteria; American Society of Anesthesiologists (ASA) grade I & II patients, age group 18-40years, undergoing elective caesarean section under general anesthesia. Patients, who had any pathology of the upper respiratory or alimentary tract or had predicted difficult endotracheal or orogastric intubation were excluded as resultant injury may lead to bleeding and would also alter the results by mixing with gastric contents. Patients, on medication in the last one

week, known to affect gastric fluid volume, pH or gastric emptying and leading to changes in gastric fluid volume and/or acidity as well as who refused to take part in the study were also excluded.

Written informed consent was taken from each patient for using their personal data in the research. Patients were explained the effects of medication and procedure while obtaining informed consent. The patients were asked not to eat solid food for at least six hours and liquids for at least three hours before surgery. No routine premedication was given. Patients were divided in group A and group B. The drugs were allocated randomly to either of the two groups. The method of randomization was the administration of drugs turn by turn i.e. first enrolled patient was given tablet erythromycin 250 mg and second patient was given Tab. Metoclopramide 10 mg one hour before surgery.

After applying standard monitoring, anesthesia was induced in each patient with inj. thiopentone (5mg/kg) and suxamethonium (1.5mg/kg). After intubation, anesthesia was maintained with oxygen and sevoflurane. Inj. atracurium was used as a muscle relaxant. Multiorificed orogastric tube (18 Fr) was passed before allowing the surgical team to proceed. In the head down position, gastric fluid was aspirated by attaching 50 ml syringe to the orogastric tube. The aspirate was measured directly from 50 ml syringe and then collected in a sterile bowl; pH was measured using a Corning digital 112 pH-meter (Corning, NY) on a portion of the sample at room temperature. The patients' data and values of residual gastric fluid volume and pH were recorded on proforma.

DATA ANALYSIS

Data were analyzed with the help of SPSS version 11. Metoclopramide and erythromycin were independent variables while gastric fluid volume and pH were dependent variables. Descriptive statistics were applied in the form of mean and standard deviation of gastric fluid volume and pH in both groups. The comparison of mean gastric fluid volume and mean pH was made among two groups. Student's T test was applied for comparison of mean and P value <0.05 was considered as significant. Chi-square test was used to generate P-values for comparison of gastric fluid volume and pH.

RESULTS

The proportion of patients with acceptable and unacceptable gastric fluid volume and pH were compared

A comparison of erythromycin and metoclopramide

according to Robert and Shirley's criteria i.e. the patient is at risk of aspiration of gastric contents when gastric fluid volume is more than 25 ml. and pH is less than 2.5. Out of total 144 patients, 21.5% patients had residual gastric volume >25 ml while 59.0% patients had gastric pH <2.5. Hence these patients were at risk of aspiration pneumonia (Tables 1, 2).

Both groups had similar patient profiles. The mean age in group A was 28.6±4.25 years while in group B it was 26.2±5.11 years. The difference in both groups was not statistically significant (p=NS).

Residual gastric volume was compared between the two groups. In group A (erythromycin) 87.5% patients had residual gastric volume less than 25 ml compared to group B (69.4%)(Tables 1&2). Statistically, difference is highly significant. P = 0.008 (P > 0.05).

The proportions of patients were also compared in terms of acceptable pH (>2.5) in the two groups. The percentage of patients with pH >2.5 was significantly higher in study group A (62.5%) as compared to B (19.4%). This was a statistically significant difference; P = 0.001 [P < 0.05].

Table 1: Comparison of gastric fluid volume in two study groups

Gastric fluid volume	Study Groups		Total	P value
	Group A N(%)	Group B N(%)		
<25 ml	63(87.5)	50(69.4)	113(78.5)	P=0.008
>25 ml	9(12.5)	22(30.6)	31(21.5)	
Total	72(100)	72(100)	144(100)	

Statistical Analysis

Chi-Square = 6.9 P=0.008 (<0.05)

Percentage of patients with gastric fluid volume <25ml was significantly higher in study group A as compared to group B.

Table 2: Comparison of pH in two study groups

PH range	Study Groups		Total	P value
	Group A N(%)	Group B N(%)		
<2.5	27(37.5)	58(80.6)	85(59.0)	P=0.001
>2.5	45(62.5)	14(19.4)	59(41.0)	
Total	72(100)	72(100)	144(100)	

Statistical Analysis

Chi-Square = 27.5 P=0.001 (<0.05)

The percentage of patients with pH more than 2.5 was significantly higher in study group A as compared to B

Table 3: Comparison of mean gastric fluid volume between two study groups

Groups	No. of Patients	Mean Aspirate volume (ml)	SD (ml)	P value
Group A	72	21.8	1.9	P=0.01
Group B	72	23.5	5.1	

Statistical Analysis

t: Value: = 2.59

P value: 0.01 (< 0.05)

Mean gastric aspirate was significantly lower in study group A as compared to B

SD = Standard Deviation

Table 4: Comparison of mean gastric fluid pH between two study groups

Groups	No. of Patients	Mean Aspirate pH	SD	P value
Group A	72	2.513	0.16	P=0.001
Group B	72	2.296	0.14	

Statistical Analysis

t: Value: = 8.67

P value: 0.001 (< 0.05)

Mean PH of gastric fluid was significantly higher in study group A as compared to B;

SD = Standard Deviation

Comparison of gastric fluid volume

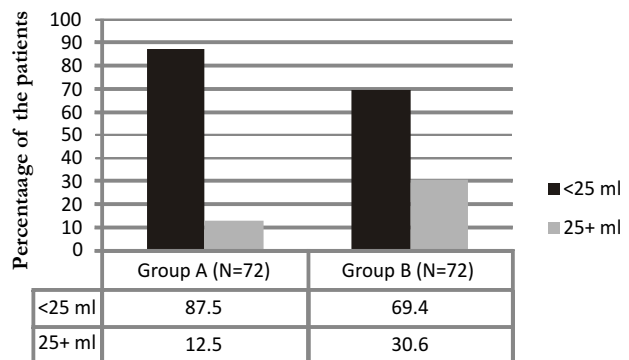


Fig I: Comparison of gastric fluid volume

DISCUSSION

Pulmonary aspiration of gastric contents during anesthesia though a rare event with an incidence of 1 in 7,000 to 8,000 in ASA I and II patients, and 1 in 400 ASA III to V patients⁸, is still considered a significant cause of anesthesia related deaths. The severity of pulmonary damage is related to both the volume and pH of the gastric fluid. A combination of volume >25 ml and pH <2.5 is considered to be a high risk.³ Complete emptying of solids from the stomach takes 5 to 6 h, but may be prolonged by fear, pain or opioids. At the time of induction of anesthesia gastric fluid volume is quite

variable in normal people. Even if the patient is fasting, the stomach is not completely empty⁷. On an average, 25 ml to 35 ml of gastric fluid remains in the stomach⁹. Comparing this to the traditional cut-off value of gastric fluid volume >25 ml and pH <2.5, patients would be at risk of pulmonary aspiration. Additionally the negative effects of progesterone during pregnancy, particularly the muscle-relaxing properties of progesterone might cause a change in the gastric emptying process. This can cause heartburn, that pregnant women frequently experience, and can lead to regurgitation.

The results of our study show that erythromycin significantly decreased the volume of gastric fluid aspirate as compared to metoclopramide group. Significant difference in pH was noted between the two groups, yet it was not significantly increased in both groups from the normal gastric pH (0.3-2.9). In both the groups under study the values were significantly lower than the values required for causing aspiration syndrome. The probability of regurgitation and aspiration of gastric contents increases during general anesthesia when the patient loses airway reflexes. Attempts have been made to manipulate the volume and pH of gastric fluid prior to the conduct of anesthesia. These maneuvers include use of overnight fast, antacids, prokinetic drugs, H₂-receptor antagonists and nasogastric aspiration. Only few prokinetic agents are available that can effectively reduce gastric fluid volume like metoclopramide by stimulating gastric emptying. Unfortunately, metoclopramide has been associated with extrapyramidal side effects. Erythromycin, a motilin receptor agonist is a macrolide antibiotic that is devoid of these side effects. It can be used as premedication for prophylaxis of aspiration pneumonia, as when given orally it has been shown to reduce both the residual gastric fluid volume as well as acidity.

Motilin, a gastrointestinal peptide whose receptors are abundant in stomach, is involved in initiating the migrating motor complex. Erythromycin, a motilin receptor agonist, is considered to induce the phase III of migrating motor complex even during the fed state. Therefore, it was likely that erythromycin significantly decreased residual gastric contents by inducing phase III and decreased gastric acidity in our study. The exact mechanism of decreasing acidity is unknown. It is likely that erythromycin decreases acidity by a direct action,

possibly through motilin receptors. Peak plasma concentration of oral erythromycin is reached in 2-3 hours. Therefore, it can be deduced that erythromycin can reduce gastric volume and acidity at much lower plasma concentration than a therapeutic concentration as an antibiotic.

Asai et al¹⁰, in their study concluded that erythromycin significantly reduced gastric volume and acidity when it was given 1 hour before induction of anesthesia than when given 3 hours before induction of anesthesia. In our study, both erythromycin and metoclopramide reduced residual gastric volume effectively in 87.5% and 69.4% patients respectively. But mean gastric fluid volume reduction was more pronounced with erythromycin as compared with metoclopramide given 1 hour before surgery.

CONCLUSION

It is concluded that oral erythromycin reduces residual gastric fluid volume more effectively than metoclopramide if given one hour before surgery. Erythromycin increases the pH of gastric fluid while metoclopramide has no effect on gastric fluid pH if given one hour before surgery. Hence erythromycin is a better option than metoclopramide in the effective reduction of gastric fluid volume and acidity.

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