

## Intravenous Rabeprazole Versus Ranitidine For Improving Preoperative Gastric Fluid Properties In Adults Under Going Elective Surgery Under General Anaesthesia - A Prospective, Randomized, Double Blind, Controlled, Clinical Study.

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### ABSTRACT

**BACKGROUND:** We compared the effect of Rabeprazole and Ranitidine given intravenously as premedication to improve the preoperative gastric fluid properties as prophylaxis against aspiration lung injury. **PATIENTS & METHODS:** The present study was conducted in 100 patients of age 18-60 years, of either sex, of ASA-PS I&II, undergoing elective surgery under general anaesthesia in a prospective double blind manner. The patients were kept fasting over night, one hour prior to surgery, patients were randomly allocated (computer generated number) in two groups. Group I received Rabeprazole (20mg) i.v. and Group II Ranitidine (50mg) i.v. One hour after the premedication, gastric contents were aspirated to record volume and pH. Quantitative data (mean±SD) of the groups were compared with student t test using graph pad in stat 3. The difference between the two groups was said to be statistically significant if  $p < 0.05$ . **RESULTS:** The administration of intravenous Rabeprazole and Ranitidine 1 hour prior to surgery is effective in reducing gastric fluid acidity and volume below the critical level (volume=25ml & pH=2.5). As compared to Rabeprazole, Ranitidine significantly decreases gastric fluid volume while both drugs show no significant difference in increasing gastric pH. **CONCLUSION:** This study shows that as compared to Rabeprazole, Ranitidine is more effective.

**Keywords-** Rabeprazole, Ranitidine, Gastric fluid volume, Gastric fluid pH

### INTRODUCTION

Induction of general anaesthesia may predispose patients to aspiration of gastroesophageal contents because of depression of protective reflexes during loss of consciousness.<sup>1</sup> Aspiration of oropharyngeal and gastric contents during surgery, although infrequent (1/4000 for elective surgery and 1/900 for emergency surgery) is a recognized and most feared complication of general anaesthesia.<sup>2</sup> Therefore averting aspiration particularly in high risk patients should be a part of preoperative plan. Various studies have concluded that gastric volume  $\geq 25$  ml and pH  $\leq 2.5$  predisposes the patient to severe lung injury, should aspiration occur.

Ranitidine, a H<sub>2</sub> receptor blocker, is an established drug to reduce gastric acidity and volume and is in routine use since long for prophylaxis of acid aspiration.<sup>3</sup> Rabeprazole is a newer, potent and fast acting proton pump inhibitor found to be superior to ranitidine in the treatment of peptic ulcer and reflux oesophagitis.<sup>4-6</sup> It has been less studied for its effects on gastric fluid properties (volume & pH), so we decided to study the comparison between Rabeprazole & Ranitidine on gastric fluid properties to minimize the risk of aspiration pneumonia.

### PATIENTS AND METHODS

After approval from the Institutional Review Board and informed written consent from the patients, this prospective, randomized, double blind, clinical study was conducted in 100 adult patients aged 18-60 years of either sex, of ASA physical status I and II scheduled for elective surgery under general anaesthesia. Patients with high risk of regurgitation - old age, trauma, emergency surgeries,

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diabetes, receiving medication affecting gastric motility, gastric acidity and volume, patients with hepatic, renal & gastro intestinal tract diseases, obese patients (BMI>25%), allergic to drug, pregnant and lactating females, tobacco chewers, smokers & alcoholics were excluded from the study. The enrolled patients were randomised using a computerised generated randomization number in two groups of 50 patients each Group 1 (n=50) - received i.v. Rabeprazole 20 mg, 1 hour prior to induction.

Group 2 (n=50) - received i.v. Ranitidine 50 mg, 1 hour prior to induction.

The patients were kept nil by mouth since 10.00 pm night before the day of surgery. On the day of surgery in the preoperative preparation room study drug was injected 1 hour before induction and then nasogastric tube (16F) was inserted into stomach. The gastric fluid samples were collected using 50 ml syringe by an anaesthesiologist who was blinded to the drug given to the patient. The volume of the gastric content was measured with a 50 ml syringe. The pH was measured using Digital pH meter of EUTECH company (figure-1). The patients with gastric fluid volume  $\geq 25$  ml and gastric pH  $\leq 2.5$  were specified at an increased risk of severe lung injury. After aspiration of gastric contents, patients were anaesthetised under standard general anaesthesia protocol. After completion of the surgery the patients were monitored for 24 hours for any side effects like nausea vomiting etc. Quantitative data (mean $\pm$ SD) of the groups were compared with student t test using graph pad in stat 3. The difference between the two groups was said to be statistically significant if  $p < 0.05$ .

**Figure 1: Eutech pH Meter.**



**RESULTS**

In this study, the demographic data of the two groups were comparable, there were no significant differences among the groups, (P>0.05) **Table 1**. There was no

statistically significant difference in the duration of fasting among the groups (P>0.05) **Table 2**. On comparison of two groups the volume of gastric content was higher in Rabeprazole than Ranitidine group (18.68 versus 15.16 ml) ( $p < 0.05$ ) difference was statistically significant **Figure 2**, while pH was higher in Ranitidine than Rabeprazole group (6.68 versus 6.12), difference was not significant statistically (P>0.05) **Figure 3**. While in **Table 3**, there were no significant differences in the incidence of nausea, vomiting & headache among the groups & no other adverse effects encountered.

**Table 1: Patients Characteristics**

Patient's Characteristics	Group 1 (Rabeprazole)	Group 2 (Ranitidine)	P value
Age (years) (Mean $\pm$ SD)	31.45 $\pm$ 10.49	32.08 $\pm$ 10.34	P>0.05
Sex(M/F)	31/19	29/21	P>0.05
Weight(Kg) (Mean $\pm$ SD)	59.48 $\pm$ 6.48	59.26 $\pm$ 6.53	P>0.05

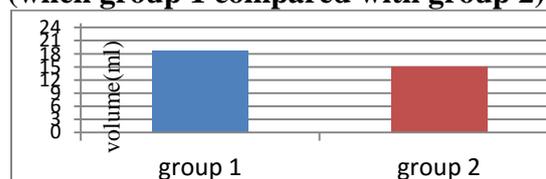
There were no significant differences among the groups (P>0.05).

**Table 2 : Duration of Fasting**

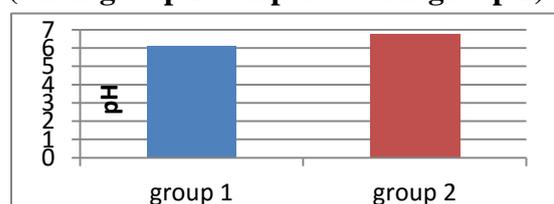
Duration of Fasting (mean $\pm$ SD)	Group 1 (Rabeprazole)	Group 2 (Ranitidine)	P value
Hours of fasting	10.50 $\pm$ 0.8	10.68 $\pm$ 0.72	P>0.05

There was no statistically significant difference in the duration of fasting among the groups (P>0.05).

**Figure 2: Gastric Fluid Volume. P<0.05 (when group 1 compared with group 2)**



**Figure 3: Gastric fluid pH. P>0.05 (when group 1 compared with group 2)**



**Table 3 : Side effects**

Side effects	Group 1 (Rabeprazole)	Group 2 (Ranitidine)
Nausea and Vomiting	3 (6%)	4 (8%)
Headache	2 (4%)	2 (4%)
Rashes	Nil	Nil
Others	Nil	Nil

There were no significant differences in the incidence of side effects in two groups.

## **DISCUSSION**

The aspiration of gastric contents can occur in patients with a depressed level of consciousness.<sup>1</sup> Pulmonary aspiration is a serious potential complication of pharmacosedation and general anesthesia. Sequelae associated with aspiration include pulmonary obstruction, chemical pneumonitis, secondary infection and possibly death. 10-30% of anesthesia related deaths occurred due to pulmonary aspiration. Morbidity following aspiration is enhanced with an increased volume of aspirate, a more acidic pH, a high particle content and bacterial contamination.<sup>7</sup> Recent guidelines on preoperative fasting published by the American society of Anesthesiologists Task force in 2011, do not recommend routine preoperative use of gastric acid secretion blockers (H<sub>2</sub>-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 no published evidence to evaluate whether reduced gastric acid secretion is associated with decreased morbidity and mortality.<sup>8</sup> Although the practice guidelines (as mentioned above) do not recommend routine use of prophylaxis in elective surgery, various studies have shown that the gastric volume >25 ml and pH <2.5 is found in fasting patients<sup>9-11</sup> hence, a pharmacological intervention in premedication which can reduce the volume of gastric content and increase the pH is rationale & should be included in routine premedication. Many pharmacological agents have been used for prevention of acid aspiration but H<sub>2</sub> receptor blockers are most commonly used. Proton pump inhibitor is another group used for reducing gastric fluid acidity and volume and is drug of choice in the treatment of moderate to severe Gastro esophageal reflux disease, hyper secretory disorders and peptic ulcers. Ranitidine is a H<sub>2</sub> receptor antagonists inhibit secretion of gastric acid, decreasing both the acidity and volume of gastric contents<sup>12</sup>. Rabeprazole is a proton pump

inhibitor, having two major differences from its predecessors. Primarily, it is a partially reversible PPI, thus there is a shorter duration of acid inhibition, secondarily, it has gastric effects other than secretory properties. It caused production of gastrin mucin. The increased intracellular mucin content suggests beneficial gastric effects. It inhibits the acid secretion provoked by histamine, pentagastrin or dibutyryl cyclic adenosine mono phosphate. The drug does not alter endocrine functions.<sup>13</sup> As the insertion of nasogastric tube is a prerequisite in our study to aspirate gastric contents for measurement of gastric fluid pH and volume, we have mostly selected laparoscopic procedures (82%) because insertion of nasogastric tube is mandatory in all laparoscopic procedures for decompressing the stomach to improve the operative visibility for surgeon. In this study blind aspiration was done to measure the volume of gastric contents, as done in other studies.<sup>10, 14- 16</sup> The technique may incompletely empty the stomach and therefore underestimates the gastric fluid volume. The alternative methods include gastric aspiration by using visually guided gastro scope, by Salem sump tube and dye dilution technique<sup>17</sup>. Aspiration using a visually guided gastro scope will give precise measurement of gastric volume but irritation by the gastro scope or insufflation of air may stimulate gastric secretion<sup>15</sup>. The double lumen Salem sump tube avoids the pulling of gastric mucosa in to the drainage eye (like a simple Ryle's tube) preventing further aspiration of gastric fluid and causing damage to gastric mucosa. The lumen Salem sump tube avoids this complication by allowing air flow through the vent lumen while gastric fluid is being aspirated through the main lumen.<sup>12,17</sup> Ryle's tube is much cheaper as compared to Salem sump tube & gastro scope, while dye dilution technique is complicated and time consuming<sup>18</sup>, so we use the Ryle's tube in the present study. Varieties of adverse reactions have been ascribed to Ranitidine, reflecting in part, the large number of patients treated with this drug. The

incidence of these reactions is small (<1%) and reactions are generally minor. Rabeprazole and Ranitidine has a low affinity to cytochrome p<sub>450</sub> system of the liver.<sup>12,13</sup> There is no interaction of Rabeprazole with antacids, antipyrine, carbamazepine, diazepam, digoxin, caffeine, diclofenac. Rabeprazole requires no dose adjustment for patients with renal insufficiency or with mild to moderate hepatic dysfunction. In this study, patients were belong to ASA physical status I and II, to ensure a safe approach to the evaluation of Rabeprazole and Ranitidine, there was no significant difference in the incidence of nausea, vomiting (6% versus 8% respectively), and headache (4% versus 4%) among the two groups and no other adverse side effects were encountered. This proves the safety of both the drugs, if used as a premedication before the surgery. Thus we concluded that, both drugs are effective in reducing gastric fluid volume and acidity below the critical value for severe lung injury should aspiration occur and their comparison clearly warrants their routine use not only in high risk patients for pulmonary aspiration but also in patients who have been fasted overnight. Ranitidine is more effective in improving gastric fluid properties than Rabeprazole & more cost effective too.

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