Study on intravenous rabeprazole and intravenous ranitidine for improving perioperative gastric fluid properties in patients undergoing elective surgery under general anesthesia

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ABSTRACT

Background: Aspiration of acid into the lungs is an infrequent but potentially devastating complication of general anesthesia. Routine practice often includes use of pharmacological agents to reduce gastric volume and increase gastric pH. The aim of the study is to compare the effectiveness of intravenous rabeprazole and intravenous ranitidine on gastric fluid properties in patients undergoing elective surgery under general anesthesia.

Materials and methods: It is a prospective study conducted on 60 patients of either sex undergoing elective surgery under general anesthesia of age group 20-70 years were two groups are assigned with, Group A received intravenous rabeprazole 20mg and group B received intravenous ranitidine 50mg on the day of surgery. Results: The volume of the gastric contents in post intubation is 4.53±1.25 mL in Group A, 5.63±1.03 mL in Group B and pre extubation is 6.10±0.84 in Group A, 8.70±2.29 mL in Group B there was significant(p<0.001) decrease in gastric volume with rabeprazole compared to ranitidine. The pH values determined in post intubation is 3.29±0.40 in Group A, 2.46±0.50 in Group B and pre-extubation is 5.28±0.48 in Group A, 4.48±0.47 in Group B there was significant(p<0.001) increase in pH with rabeprazole compared to ranitidine. Conclusion: This study concludes that the prophylactic intravenous administration of rabeprazole is more effective than ranitidine for reducing gastric volume and improving gastric pH.

Keywords: General anaesthesia, Aspiration, Gastric volume, Gastric pH

Introduction

Pulmonary aspiration of oropharyngeal and gastric content during surgery although infrequent (1/4000 in elective surgery and 1/900 in emergency surgery) is a recognized complication of general anaesthesia because of depression of protective reflexes due to loss of consciousness[1].

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Aspiration has been recognized for more than 2000 years. Aspiration syndrome is known as “Mendelson’s syndrome” and this is airway obstruction by solid material or liquid aspiration which resulted in intense inflammatory reaction of the lung tissue manifesting as bronchospasm, pulmonary edema and hypoxia[2]. Aspiration of the gastric contents of the lungs accounts for at least 10-20% of deaths attributable to anaesthesia due to aspiration pneumonitis, ARDS, pulmonary edema[3]. Silent regurgitation of small amounts of gastric contents into the oropharynx occurs in 4-26% of all cases under general anesthesia[4]. Mortality rate of ARDS is as high as 50% concerned with aspiration in conditions like pregnancy, obesity, gastroparesis etc. Patients especially undergoing upper abdominal surgery present a greater risk during induction and recovery[5]. Acid aspiration syndrome (AAS) occurs mainly during general anesthesia, regional techniques are the most
Rabeprazole reacts with sulfhydryl groups of proton pump in stimulatory process for acid secretion. Active form of resulting in inhibition of acid formation. Rabeprazole secretory surface of parietal cell and acts on the final step of gastric secretion by inhibiting H+/K+ ATPase in gastrointestinal tract. Rabeprazole, a substituted benzimidazole derivative is an effective prophylactic measure. Measures and maneuvers to prevent aspiration of acid gastric contents during general anesthesia include preoperative fasting, non-particulate antacids, H2 receptor blockers, gastro kinetic drugs like metaclopramide, rapid-sequence induction with cricoid pressure and awake extubation during emergence from general anesthesia[6]. Maternal mortality has dramatically declined in the recent times because of the new fasting regimens, increasing use of regional anesthesia for cesarean section, and the universal adoption of Sellick’s maneuver for aspiration prophylaxis. 2 Out of 8,155 patients who underwent emergency obstetrical or gynecological surgery under anesthesia and 7,473 patients who underwent elective surgery under anesthesia, there were only two cases of pulmonary aspiration which were managed successfully[7]. Clinical consequences of aspiration are varied. Primary determinants are the nature and volume of material aspirated and host responses to it[1].

Aspiration of gastric contents with pH <2.5 and volume >25 ml (or)>0.4 ml/kg causes extensive lung damage[7]. Some studies suggest that pH>3.5 can also cause pulmonary damage[6]. Gastric acidity may be at its greatest peak following overnight fasting and when patient comes to operation theatre for elective surgery there are greater chances of aspiration due to anxiety[6]. The main factor that determined the risk of aspiration pneumonitis is pH of the aspirated material[7]. Antacids are effective in raising gastric pH above 2.5 in most patients but there are problems associated with their use. They are short acting, increase the volume of gastric contents, may not mix adequately with gastric fluid and can cause nausea and diarrhea. Anticholinergics and metaclopramide were also tried. Histamine-2 receptors antagonists such as cimetidine, ranitidine and famotidine tested as prophylactic agents have been proved to be effective[9]. Ranitidine is a H2 receptor antagonist that inhibits competitively at parietal cell H2receptor and reduces acid secretion in a linear, dose dependent manner. H2receptor antagonists reduce acid secretion stimulated by histamine as well as by gastrin and cholinomimetic agents. They are especially effective at inhibiting nocturnal acid secretion[8].

Proton pump inhibitors (PPI’s) have been extensively used for healing of peptic ulcers and found superior to Histamine receptor-2 antagonist (H2 receptor blockers). Rabeprazole, a substituted benzimidazole derivative is an irreversible proton pump inhibitor which decreases gastric secretion by inhibiting H+/K+ ATPase in secretory surface of parietal cell and acts on the final step in stimulatory process for acid secretion. Active form of rabeprazole reacts with sulfhydryl groups of proton pump resulting in inhibition of acid formation. Rabeprazole inhibits acid secretion provoked by histamine, pentagastrin, dibutyryl cyclic AMP. Experimentally rabeprazole has shown to increase intracellular mucin content and new mucin synthesis in gastric mucosa[8]. Aim of our study is to compare the effectiveness of intravenous rabeprazole 20mg and intravenous ranitidine 50mg on gastric fluid properties in patients undergoing elective surgery under general anesthesia.

**Methodology**

This is a prospective study conducted in P.E.S. Institute of Medical Sciences & Research on 60 patients of either sex undergoing elective surgery under general anesthesia.

**Inclusion criteria:** Age group 20-70years, either sex, ASA physical status Grade I &II, posted for elective surgery under general anesthesia.

**Exclusion criteria:** Patients with ASA Grade III &IV, patients with GERD, patients with peptic ulcer, patients with delayed gastric emptying, patients on treatment with PPI’s and drugs affecting gastric motility, patients with hypersensitivity to drugs, patients with occurrence of nasal bleeding during nasogastric tube insertion, patients with upper gastrointestinal tract disease.

After a thorough pre anaesthetic evaluation, the patients were kept fasting of 8-12hrs before the day of surgery. They were assigned to two groups, Group A received intravenous rabeprazole 20mg and group B received intravenous ranitidine 50mg on the day of surgery. An appropriate size ryles tube (nasogastric tube) was passed in all patients one and half hour before the surgery in the preoperative room. The correct position was confirmed by auscultation over epigastrium. Gastric aspiration of fasting sample was done as soon as nasogastric tube is passed. The volume and pH of the first sample was analysed with pH meter. The patient’s vitals such as blood pressure, pulse rate, Spo2 were recorded and shifted to the operating room.

In the operation theatre all patients receive inj.glycopyrolate as premedication. Inj.fentanyl 2mcg/kg was given for analgesia. Following preoxygenation for three minutes, anesthesia was induced with inj. Thiopentone 4-5 mg/kg and inj. succinylcholine 1.5mg/kg was given to facilitate tracheal intubation. Cricoid pressure was applied at loss of the eyelash reflex. Cuffed endotracheal tube of appropriate size was used for intubation and its position was confirmed with auscultation and capnography. After fixation of E.T tube gastric aspirate sample was collected and its volume and pH were recorded. Neumoruscullar blockade was achieved with inj.vecturonium 0.1 mg/kg. Anesthesia was maintained with...

maintained with 66% N2O, 33% O2&0.5-1% halothane. At the end of surgery, inj. neostigmine and inj. glycopyrolate were given to reverse the residual neuromuscular blockade. Just before extubation third sample was collected to record volume of the gastric aspirate and its pH.

Results

Comparisons between groups were made using Student's t test for age and fasting period. Analysis of variance was used for comparison of gastric pH and volume and "t" test with Yates correction for incidence of patients at risk of acid aspiration syndrome. The values were considered to be statistically significant at P <0.05.

Table 1: Age distribution of patients in study

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Group-A</th>
<th>Group-B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>&lt;20</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>21-30</td>
<td>13</td>
<td>43.1</td>
</tr>
<tr>
<td>31-40</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>41-50</td>
<td>5</td>
<td>16.7</td>
</tr>
<tr>
<td>51-60</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>61-70</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>36.97±13.13</td>
<td>40.23±13.87</td>
</tr>
</tbody>
</table>

Figure 1: Demographic distribution in study

Table 2: Gender distribution of patients studied

<table>
<thead>
<tr>
<th>Gender</th>
<th>Group-A</th>
<th>Group-B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
<td>23.3</td>
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<tr>
<td>Female</td>
<td>23</td>
<td>76.7</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100</td>
</tr>
</tbody>
</table>

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Table 3: Physical status: ASA Grade

<table>
<thead>
<tr>
<th>Physical status</th>
<th>Group-A</th>
<th>Group-B</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA Grade</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Grade-I</td>
<td>29</td>
<td>96.7</td>
</tr>
<tr>
<td>Grade-II</td>
<td>1</td>
<td>3.3</td>
</tr>
</tbody>
</table>

Table 4: Comparison of Pre intubation, Post intubation & Pre- Extubation of gastric volume (milliliter) in two groups

<table>
<thead>
<tr>
<th>Intubation</th>
<th>Group-A</th>
<th>Group-B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre intubation</td>
<td>15.03±1.92</td>
<td>15.37±37</td>
<td>0.28</td>
</tr>
<tr>
<td>Post intubation</td>
<td>4.53±1.25</td>
<td>5.63±1.03</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Pre Extubation</td>
<td>6.10±0.84</td>
<td>8.70±2.29</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

*p-value significant.
Table 5: Comparison of Pre intubation, Post intubation & Pre extubation of pH in two groups studied

<table>
<thead>
<tr>
<th>Intubations</th>
<th>Group-A</th>
<th>Group-B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre intubation</td>
<td>1.85±0.20</td>
<td>1.78±0.23</td>
<td>0.273</td>
</tr>
<tr>
<td>Post intubation</td>
<td>3.29±0.40</td>
<td>2.46±0.50</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Pre Extubation</td>
<td>5.28±0.48</td>
<td>4.48±0.47</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

*p-value significant.

Discussion

Pulmonary aspiration of gastric contents during anesthesia particularly during induction, intubation and recovery is a small but important cause of anesthesia related deaths. Although precise numbers are not known, it is probable that many patients suffer nonfatal aspiration with considerable morbidity. Any safe treatment that reduces this hazard is desirable. Efforts at reducing the complications of acid aspiration syndrome initially focused increasing gastric pH > 2.5 with oral antacids given before general anesthesia. However, antacids are reported to increase gastric volume besides the particulate matter in the antacids increase the complications if aspiration occurs. Various clinical reports described severe pulmonary disturbances and even death following aspiration of gastric contents containing antacids. Administration of H2 receptor antagonists increases gastric pH and decreases gastric volume.3

Ranitidine is a H2 receptor antagonist that inhibits competitively at parietal cell and reduces acid secretion. Rabeprazole decrease gastric secretion by inhibiting the activity of H+/K+ ATPase. We preferred to administer intravenous ranitidine 50mg and intravenous rabeprazole 20 mg because this offers the advantage of improved bioavailability compared to oral administration, where delayed gastric emptying might render oral medication less effective when it is most required.

In present study volume of the gastric contents in post intubation is 4.53±1.25 mL in Group A, 5.63±1.03 mL in Group B and pre extubation is 8.70±2.29 mL in Group B there was significant(p<0.001) decrease in gastric volume with rabeprazole compared to ranitidine. The pH values determined in post intubation is 3.29±0.40 in Group A, 2.46±0.50 in Group B and pre-extubation is 5.28±0.48 in Group A, 4.48±0.47 in Group B there was significant(p<0.001) increase in pH with rabeprazole compared to ranitidine. Our study correlates with other studies done previously[9,10].
Study done by Takanobu uesugi, et al (2002) concluded that morning dose of oral lafutidine 20mg seem to be more effective in decreasing gastric fluid acidity and volume than oral ranitidine 150 mg[11]. The positive effect of ranitidine in reducing gastric volume and acidity as concluded in our study as opposed to the study of above authors is probably because ranitidine has been used intravenously and not orally.

In study done by Kahoru Nishina et al (2002) found that single dose of ranitidine 150 mg orally was the most effective regimen to control gastric fluid property and administration of two consecutive doses of rabeprazole 20 mg was the second most effective remedy and rabeprazole has minimal indication for prophylaxis of acid aspiration syndrome[12].

In the study done by above authors ranitidine was more effective than rabeprazole to control gastric fluid property and volume. In our study rabeprazole have been more effective as it is used intravenously. The oral rabeprazole has enteric coating which causes delay in absorption[12].

In a study done by Escolano.F, et al in (2003) concluded that ranitidine or Famotidine is better than omeprazole in reducing gastric fluid properties[13]. The study is in partial agreement with the present study to establish the fact some form of H2 receptor antagonists or proton pump inhibitors given preoperatively will give adequate protection against complications of active or passive aspiration supported by other studies[14].

In a study done at Dehradun hospital in India in the year 2008 by Gurkaran kaur Sidhu, et al concluded that administration of i.v pantoprazole when compared to i.v ranitidine was associated with most appreciable changes in characteristics of gastric content and is most efficient for decreasing chances of mendelson syndrome[15]. The above study has been in total agreement with the present study done to conclude that proton pump inhibitor used preoperatively will appreciably change the characteristic of gastric content.

Jan Muhammad Shaikh, et al assessed anesthetic practice patterns and measures to prevent aspiration of acid gastric contents in full term pregnant women undergoing anaesthesia for Caesarean section. Authors noticed 90% of anesthetists used acid aspiration prophylaxis by H2 blockers and proton pump inhibitors[6].

Tapas Bhattacharyya, Debabrata et al in 2011 inferred that ranitidine is more effective than pantoprazole to raise the gastric pH for prevention of aspiration pneumonitis[16]. The study is in partial agreement with our study in which we have concluded that proton pump inhibitor rabeprazole is superior to H2 receptor antagonist ranitidine in reducing gastric fluid acidity and volume for prevention of aspiration pneumonitis. This slight difference in inference may be due to lowest critical value for pH considered in our study as compared to study by above authors.

Conclusion

This study concludes that the prophylactic intravenous administration of rabeprazole is more effective than ranitidine for reducing gastric volume and improving gastric pH. Therefore even if a gastric aspiration occurs inspite of all precautions during general anaesthesia, the complications and ill effects of Mendelson’s syndrome will be far less if intravenous rabeprazole is used as prophylactic in preoperative period than when intravenous ranitidine is used. The improvement in gastric pH and reduction in gastric volume by rabeprazole was statistically significant.

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