The Effect of Famotidine on Lowering Gastric Acidity in Gastric Carcinoma Patients

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= Abstract =

Background: To identify the gastric pH of gastric carcinoma patients after more than 8 hours of fasting and ascertain the antisecretory effects of H₂-receptor antagonists, the gastric volume and pH of 41 gastric carcinoma patients was checked immediately after the induction of inhalational general anesthesia (endotracheal intubation).

Methods: The patients were divided randomly into two groups: the control received IV normal saline as a placebo and the famotidine group received IV famotidine as a premedicant 1 to 2 hours before the induction of anesthesia. Immediately after the induction of anesthesia, the gastric contents were aspirated blindly with a 60 ml syringe. Fisher's exact test was used to compare the percentage of patients 'at risk' between the two groups in relation to their pH and volumes.

Results: The percentage of patients 'at risk' (volume > 0.4 ml/kg and pH < 2.5) of acid aspiration pneumonitis in the control and famotidine groups was 8.7% and 5.6%, respectively, which was 30–77% lower than for patients with no premedication, as observed in other studies. In the present study, the difference in percentage of patients 'at risk' between the two groups was not statistically significant.

Conclusions: The gastric carcinoma patients exhibited a higher gastric pH when fasting and a lower risk of acid aspiration pneumonitis relative to their gastric contents. The effect of famotidine on lowering gastric acidity and volume in gastric carcinoma patients was rather weak. Accordingly, the routine use of H₂-receptor antagonists to decrease gastric secretion in gastric carcinoma patients should be reevaluated. (Korean J Anesthesiol 2000; 38: S1–S5)


INTRODUCTION

The regurgitation and subsequent aspiration of gastric contents during anesthesia can be associated with serious aspiration pneumonia. It has been suggested that a patient is 'at risk' of aspiration pneumonitis when their gastric pH is lower than 2.5 and their gastric volume is greater than 0.4 ml/kg.\(^1\) The preanesthetic agents used to prevent acid aspiration pneumonitis through their reduction of acid secretion include various H₂-receptor antagonists,\(^2\) of which, famotidine is known to be the most potent and long acting, with fewer side effects,\(^3\) however, it does...
decrease the stroke volume of the left heart.\(^4\)

It is well known that patients with gastric carcinoma have a relatively high gastric pH which is associated with precancerous lesions, such as atrophic gastritis or achlorhydria.\(^5\) Shearman\(^6\) reported that the depression of acid secretion and intrinsic-factor secretion are both impaired in patients with gastric carcinoma.

The present study was conducted to identify the pH of gastric juices during a state of fasting and evaluate the inhibitory effect of famotidine on gastric acid secretion in gastric carcinoma patients.

**METHODS**

This study was conducted on 41 gastric carcinoma patients identified by the American Society of Anesthesiologists as Classification I or II (ASA I or II), aged between 20–65, and undergoing elective subtotal or total gastrectomy. The protocol was approved by the ethical committee of Kosin medical college, and written informed consent was obtained from all patients. The patients were randomly assigned to one of 2 groups: the control group (n = 23) received a placebo intravenously as a premedicant and the famotidine group (n = 18) received 20 mg of famotidine. The drugs were intravenously administered as a bolus 1 to 2 hours before the induction of anesthesia. Any patients with apparent cardiovascular, pulmonary, and endocrinologic diseases, or those who were pregnant, hypersensitive to drugs, or receiving antacids or other \(\text{H}_2\)-receptor antagonists were excluded. In addition, patients who showed signs of gastric obstruction or who had preoperatively-inserted nasogastric tubes were also excluded.

The study was carried out in a double-blind manner. The anesthesia was induced with glycopyrrolate 0.2 mg i.v. and thiopental sodium 4–5 mg/kg i.v., and succinylcholine chloride 1–1.5 mg/kg i.v. was used to facilitate endotracheal intubation. The anesthesia was maintained with 50% nitrous oxide in oxygen supplemented with volatile agents or potent narcotics. Pancuronium bromide or vecuronium bromide was used as a muscle relaxant. Immediately after the induction of anesthesia, a size 16 or 18 French gauge nasogastric tube (All-silicone gastric duodenal levintube\(^7\), Sewoon Medical Co., Seoul, Republic of Korea) was inserted into the stomach and the accuracy of its position was verified by either the aspiration of the gastric contents or the auscultation of the injected air. The gastric contents were aspirated blindly with a 60 ml syringe fitted tightly to the proximal end of the nasogastric tube, meanwhile the abdomen was manually compressed near the stomach and the patient’s position changed from side to side. When the abdominal cavity was subsequently open, the position of the tube was checked by the surgeon and the gastric emptying was then completed manually while the patient continued to aspirate through the gastric tube. The total volume and pH of the gastric samples were measured. The gastric volume was indexed to the body weight (ml/kg). The pH was determined using a pH microelectrode (pH meter\(^8\), Beckman Inc., CA, USA), calibrated prior to each determination.

The patient’s age, weight, and the pH and volume of the gastric fluid aspirate were presented as a mean ± SD. The parametric data was analyzed using the Mann-Whitney U-test. Patients with a gastric volume > 0.4 ml/kg and a pH < 2.5 were classified as being ‘at risk’ of acid aspiration pneumonitis. Fisher’s exact test was used to compare the percentage of patients ‘at risk’ between the two groups in relation to their pHs and volumes. The differences were considered statistically significant when the P values were less than 0.05.

**RESULTS**

There were no significant differences between the two groups with regard to sex distribution, age, and weight. The mean gastric pH of the control group (gastric juices in fasting gastric carcinoma patients) was 4.6 ± 2.1, which is higher than the normal reference value (1.5–3). The mean gastric pH of the
Table 1. Demographic Data

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Famotidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>51.9 ± 12.2</td>
<td>53.3 ± 11.7</td>
</tr>
<tr>
<td>Sex (m/f)</td>
<td>11/12</td>
<td>12/6</td>
</tr>
<tr>
<td>Wt (kg)</td>
<td>57 ± 6.0</td>
<td>60.9 ± 9.6</td>
</tr>
<tr>
<td>pH</td>
<td>4.6 ± 2.1</td>
<td>5.5 ± 2.0</td>
</tr>
<tr>
<td>Volume (ml)</td>
<td>17.4 ± 12.3</td>
<td>17.8 ± 13.6</td>
</tr>
<tr>
<td>Interval (min)*</td>
<td>62.3 ± 22.6</td>
<td>65.7 ± 24.9</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD or number. There were no significant differences between the two groups according to a Mann-Whitney test. *: Interval between drug administration and gastric aspiration.

Table 2. Distribution of pH of Gastric Juice

<table>
<thead>
<tr>
<th>Group</th>
<th>pH &lt; 2.5</th>
<th>pH &gt; 2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>6 (26%)</td>
<td>17 (74%)</td>
</tr>
<tr>
<td>Famotidine</td>
<td>3 (17%)</td>
<td>15 (83%)</td>
</tr>
</tbody>
</table>

There was no significant difference between the two groups according to a Fisher's exact test.

Table 3. Distribution of Volume of Gastric Juice

<table>
<thead>
<tr>
<th>Group</th>
<th>Volume &lt; 0.4 ml/kg</th>
<th>Volume &gt; 0.4 ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16 (70%)</td>
<td>7 (30%)</td>
</tr>
<tr>
<td>Famotidine</td>
<td>14 (78%)</td>
<td>4 (22%)</td>
</tr>
</tbody>
</table>

There was no significant difference between the two groups according to a Fisher's exact test.

The interesting result from the present study is that the percentage of patients 'at risk' (with volume > 0.4 ml/kg and pH < 2.5) was only 8.7% in the control group and 5.6% in the famotidine group, which is considerably lower by 30–77% compared with other studies. There was no significant difference in the 'at risk' percentages between the control and famotidine groups in the present study. The mean gastric pH (4.6) of the gastric carcinoma patients in the control group was higher than the normal reference value, however, the gastric volumes (17.4 ml) observed in this study are similar to those reported for overnight fasting subjects in other studies. In the famotidine group, the famotidine, a H2-receptor antagonist, was intravenously administered to lower the acidity of the gastric contents 60–90 minutes before the induction of anesthesia. However, their gastric juice volumes and pHs were not significantly different.

DISCUSSION

The proportion of patients 'at risk' (pH < 2.5 and volume > 0.4 ml/kg) was 8.7% in the control and famotidine groups were 8.7% (2/23) and 5.6% (1/18).
from those of the control group.

Shearman\textsuperscript{6} observed a depressed acid and intrinsic-factor secretion and a high incidence of hypochlorhydria and achlorhydria in gastric carcinoma patients. Accordingly, he suggested that the gastric pH in gastric carcinoma patients could be more alkalotic than normal. Furthermore, gastric diseases with lower acid secretion, such as atrophic gastritis and hypochlorhydria, generally produce gastric carcinoma pre-cancerous lesions.\textsuperscript{5} The current study found that the pH of the gastric juice of gastric carcinoma patients was more alkalotic than in subjects with no gastric carcinoma.

The aspiration of gastric contents continues to be a major cause of morbidity and mortality related to anesthesia.\textsuperscript{10} Acid aspiration pneumonitis during anesthesia, especially, during the induction of anesthesia, is a preventable iatrogenic complication. It is generally accepted that patients with a gastric volume $> 0.4$ ml/kg and a pH $< 2.5$ at the time of induction are at risk of acid aspiration pneumonitis, and the higher the acidity, the less the volume required to cause pulmonary damage.\textsuperscript{11} The severity of the pulmonary lesions following the aspiration of gastric contents appears to be critically dependent on the acidity of the aspirate. In order to reduce this risk, it is necessary to raise the gastric pH and decrease the gastric content. A number of methods have been tested to achieve this including the use of an H$_2$-receptor antagonist as a preoperative medication.

Several studies have demonstrated the beneficial effects of the preoperative administration of H$_2$-receptor antagonists in reducing gastric volume and acidity.\textsuperscript{12-15} Famotidine, a potent H$_2$-receptor antagonist, appears to be more effective than cimetidine and ranitidine and has fewer side effects and drug interactions.\textsuperscript{3} Preanesthetic medication with oral, intravenous, and intramuscular famotidine increases the gastric pH and lowers the gastric volume.\textsuperscript{7,16} The effect of famotidine on increasing the gastric pH begins within 30 minutes\textsuperscript{17} of a premedicant intravenous injection, a significant suppression can be noted as early as one hour after the drug administration,\textsuperscript{18} and the total effect lasts 10 to 12 hours. An intravenous dose of famotidine is twice as potent as an oral dose.\textsuperscript{19} Theoretically, famotidine should also increase the sedative effect of midazolam, with few side effects, however, constipation, diarrhea, headache, tinnitus, and cutaneous rashes can be induced. Mescheder et al.\textsuperscript{4} insisted that famotidine (40 mg) causes a significant fall in stroke volume and cardiac output due to a negative inotropic effect. The hospital associated with this research routinely administers H$_2$-receptor antagonists to patients with gastric carcinoma in order to decrease the acidity of their gastric contents. More recently, IV famotidine has been used as a preoperative medication. Even though side effects of famotidine are rarely reported, several patients have been observed to become hypotensive when they arrived at the operating room, although their blood pressure was normal in the wards. They had no previous cardiovascular or endocrinologic problems which can cause hypotension and bradycardia, other than a light cachexia. The routine use of these agents can induce a false sense of security for anesthesiologists and reduce their vigilance, whereas clinical studies have not yet established the benefit of using H$_2$-receptor antagonists before elective surgery.\textsuperscript{19} Accordingly, the use of famotidine as a premedicant to prevent acid aspiration pneumonitis in gastric carcinoma patients needs to be further evaluated.

In this study, several patients who showed signs of gastric obstruction due to gastric mass were excluded as their gastric juice had been drained a result of the previous insertion of a nasogastric tube to decompress the distention of the stomach. However, in hindsight, the gastric pH of these fasting patients should have been checked and not excluded.

In summary, the gastric carcinoma patients in the present study showed a higher gastric pH in a fasting state compared with previously reported results, irrespective of the use of IV famotidine as a premedicant. Moreover, the antisecretory effect of H$_2$-receptor antagonists was more suppressed in gastric carcinoma
patients, and thus the validity of famotidine pre-
médication in the gastric carcinoma patients should be
re-evaluated. The effect of famotidine in the suppres-
sion of gastric acid secretion in gastric carcinoma
patients needs further study.

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