The effect of oral Bicitra® compared with intramuscular cimetidine on gastric volume and pH in outpatient surgery

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A comparison is made between the effectiveness of oral Bicitra® (sodium citrate) and intramuscular cimetidine in increasing the pH and reducing the volume of the gastric fluid in unpremedicated adult outpatients. Patients were assigned randomly to three groups. Group I received 15 ml oral Bicitra® 15 minutes prior to induction of anesthesia. Group II received 300 mg cimetidine intramuscularly 30 minutes prior to induction, and Group III served as the control. Gastric fluid was analyzed for pH and volume. The cimetidine group had a significantly higher gastric pH and reduced gastric volume when compared with the Bicitra® and control groups (p<0.001). The Bicitra® group had a significantly higher pH and volume compared with the control group (p<0.001).

This study compares the effectiveness of oral Bicitra® (sodium citrate) with intramuscular cimetidine in increasing the pH and reducing the volume of the gastric fluid contents in unpremedicated adult surgical outpatients.

Forty-five patients were assigned randomly to one of three groups upon arrival at the outpatient department. Those in Group I (N=15) received a single oral 15 ml dose of Bicitra® 15 minutes prior to the induction of anesthesia. Those in Group II (N=15) received a single intramuscular 300 mg dose of cimetidine 30 minutes prior to the induction of anesthesia. Patients in Group III (N=15) served as a control and received neither Bicitra® nor cimetidine.

Following anesthetic induction and endotracheal intubation, an orogastric tube was placed, and gastric residuals were obtained for pH and volume. One-way analysis of variance (p<0.001) and a Bonferroni t-test (p<0.05) revealed a significantly higher gastric pH and reduced gastric volume in the cimetidine group compared with the Bicitra® and control groups (p<0.001).

There was a significantly higher gastric pH in those subjects receiving Bicitra® when compared with the control group (p<0.001), but gastric volume was increased significantly within the Bicitra® group. There was no statistical linear correlation between weight, number of hours fasted and type of surgery on the gastric pH and volume within the three groups (p<0.001).

Introduction

Acid pulmonary aspiration (Mendelson's) syndrome is a well-recognized complication in patients undergoing general anesthesia. It has been documented that the patient at increased risk possesses a gastric volume exceeding 0.4 ml/kg of body weight or a minimum of 25 ml and a gastric pH of 2.5 or less. Prophylactic preoperative oral administration of antacids has been shown to reduce preoperative gastric acidity in many patients. However, the inhalation of emulsion-type antacids may
produce extensive and prolonged pathologic changes because of the particulate nature of these antacids. Bicitra®, a palatable form of sodium citrate, a non-particulate solution, has been proposed as an acceptable, inexpensive alternative. Timing of administration and increasing gastric volume are important considerations with oral solutions.

An alternative to oral solutions is an H₂ histamine receptor antagonist, such as cimetidine, which inhibits gastric acid secretion by blocking gastric histamine receptors.

This study was designed to investigate the effects of preoperative intramuscular administration of cimetidine compared with oral administration of Bicitra® on gastric volume and acidity in unpremedicated adult ambulatory surgical patients.

**Methods**

Forty-five adult unpremedicated female ambulatory surgical patients ranging in age from 18-58 years were studied. All were ASA I or II and scheduled for elective outpatient surgical procedures that included diagnostic laparoscopy, laparoscopic bilateral tubal ligation and breast biopsy performed under general endotracheal anesthesia.

The study was approved by the university’s committee on the conduct of human research, and informed consent was obtained from all the patients. Each subject received written instructions to restrict oral intake after midnight on the day of surgery.

Patients were assigned randomly to one of three treatment groups: control, Bicitra® or cimetidine. Patients in the Bicitra® group received a single 15 ml oral dose 15 minutes prior to the induction of anesthesia. In the cimetidine group, patients received a single 300 mg intramuscular dose 30 to 60 minutes prior to the induction of anesthesia. Patients in the control group received neither Bicitra® nor cimetidine. All patients had negative histories of disease or drug ingestion, which are known to alter gastric secretion. Sedative or anticholinergic medication was not administered to the patients prior to surgery.

Anesthesia was induced in a modified rapid-sequence manner, with preoxygenation for four deep breaths followed by intravenous d-Tubocurarine, 0.06 mg/kg, 100 μg-fentanyl, methohexital 1.5 mg/kg and succinylcholine chloride, 1.5 mg/kg, followed by immediate endotracheal intubation. Anesthesia was maintained using 70% N₂O and 30%O₂, fentanyl and isoflurane.

Immediately after tracheal intubation, a no. 16 French Salem Sump orogastric tube was placed in the stomach, and gastric contents were aspirated, measured and analyzed. Proper positioning of the gastric tube was ascertained by epigastric auscultation during air insufflation. The gastric fluid pH of the immediate postintubation aspirate was measured using a no. 125 Corning digital pH meter with a microelectrode probe combination. The pH meter was recalibrated prior to each use with a two-point analysis utilizing pH 4 and 7 buffering solutions. Gastric volume was measured with a 100 ml graduated glass cylinder.

Statistical analysis of results involved one-way analysis of variance, a Bonferroni t-test and Spearman’s rank order correlation coefficient, when appropriate. The p < 0.05 level was considered statistically significant. The mean of the pH values (not H⁺) was calculated.

**Results**

A summary of the characteristics of the three groups is shown in Table I. There were no significant differences among the three groups in age, weight, height, number of hours fasted or type of surgical procedures performed (p <0.001). By contrast, a one-way analysis of variance (p <0.001) and a Bonferroni t-test (p <0.05) revealed a significant difference in gastric pH and volume among the three groups. The data are summarized in Table II.
ever, there was a significantly higher gastric pH and reduced gastric volume in the cimetidine group compared with the other two groups ($p<0.001$). There also was a significantly higher gastric pH in those subjects receiving Bicitra® compared with those in the control group ($p<0.001$), but gastric volumes were increased significantly within the Bicitra® group. All patients in the control group had gastric pHs well below the critical level of 2.5 with significant gastric volumes.

According to Spearman's rank order correlation coefficient, there was no relationship on the basis of weight, number of hours fasted and type of surgery in the gastric pH and volume among the three groups. For both the Bicitra® and cimetidine groups, the relationship between time of drug administration and gastric volume demonstrated a random variation. A linear, cubic or quadratic relationship does not fit gastric volume and time.

By defining a patient's risk for aspiration pneumonitis based on a gastric fluid pH of less than 2.5 and a gastric volume exceeding 0.4 ml/kg of body weight, or 25 ml, the Bicitra® group demonstrated 26% of patients to be at risk; the cimetidine group 0%, and the control group 80%. (Table III). The distribution of patients with a gastric pH of less than 2.5 showed the Bicitra® group to have 26% at risk, the cimetidine group 0% and the control group 100%. The distribution of patients with a gastric volume exceeding 0.4 ml/kg, or 25 ml, revealed the Bicitra® group to be 93% at risk, the cimetidine group 6% and the control group 80%.

**Discussion**

This study demonstrates that a potential risk of acid aspiration pneumonitis exists in unpremedicated adult ambulatory surgical patients despite overnight fasting. All patients in the control group had gastric pHs of less than 2.5, with significant increases in gastric volumes. Ong and associates demonstrated that the unpremedicated elective surgical outpatient has almost twice the gastric volume of the premedicated elective surgical inpatient, with an average gastric pH of 1.8 $\pm$ 0.2. The large acidic gastric volume of outpatients may be explained by the anxiety associated with the minimal amount of preparation they get prior to surgery and not receiving any premedication.

In 1946, Mendelson was the first to demonstrate that the acidity of gastric aspirate was the major etiologic factor in aspiration pneumonitis. Subsequent experimental work by Teabeaut, Roberts and Shirley substantiated Mendelson's work and also suggested that the patient most at risk for aspiration pneumonitis has a volume of gastric contents greater than 0.4 ml/kg of body weight with a

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<th>Table II</th>
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<td><strong>Gastric pH and volume of Bicitra®, cimetidine and control groups (Mean ±SD)</strong></td>
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<table>
<thead>
<tr>
<th>Number (Pts)</th>
<th>Volume (ml)</th>
<th>pH (units)</th>
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<tbody>
<tr>
<td>*Mean ± SD</td>
<td>Range</td>
<td>*Mean ± SD</td>
<td>Range</td>
</tr>
<tr>
<td>Bicitra®</td>
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<td>61.80±25.4</td>
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</tr>
<tr>
<td>Cimetidine</td>
<td>15</td>
<td>12.33±08.5</td>
<td>6-034</td>
</tr>
<tr>
<td>Control</td>
<td>15</td>
<td>44.67±14.1</td>
<td>23-068</td>
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*Bonferroni t-test: All three groups significantly different at $p = .05$ |

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<th>Table III</th>
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<td><strong>Distribution of patients with a pH of &lt; 2.5 and a gastric volume of &gt; 0.4 ml/kg</strong></td>
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<thead>
<tr>
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<tbody>
<tr>
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</tr>
<tr>
<td>Cimetidine</td>
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<tr>
<td>Control</td>
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gastric pH of less than 2.5. Various methods to reduce the risk of aspiration have focused on reducing gastric acidity before the induction of anesthesia. Administration of oral antacids, anticholinergics and antihistamine drugs has been used for this purpose, all with variable success.

The safety of prophylactic antacid administration has been put into question by reports of significant pulmonary morbidity and mortality following aspiration of emulsion-type antacids. Eyler compared the effects of aspiration of a particulate antacid (Mylanta®) with a non-particulate Bicitra® in rabbits.

Bicitra®, a clear, soluble non-particulate antacid containing 0.3 molar sodium citrate and 0.6 molar citric acid in a sugar-free base, was shown to produce minimal pulmonary pathology after aspiration. Bicitra® is a more palatable form of sodium citrate, with a pH of 4.2, compared to sodium citrate with a pH of 8.4.

The efficacy of antacid therapy depends upon the time allowed for neutralization and gastric fluid volume. In this present study, oral administration of 15 ml of Bicitra® 15 minutes prior to the induction of anesthesia was utilized effectively, increasing the gastric pH to a level of more than 2.5 in 73% of the patients studied. However, in those same patients, 93% had gastric volumes exceeding 0.4 ml/kg of body weight.

As Stoelting noted, the neutralization of gastric contents is achieved reliably with non-particulate antacids, but a disadvantage is that the decrease of acidity occurs at the cost of increased gastric volume. As demonstrated in this study, Bicitra® did, in fact, increase gastric volumes significantly (p<0.001) when compared with the volumes of patients in the control group.

A number of studies have evaluated the efficacy of cimetidine, a competitive H₂ histamine receptor antagonist, as premedication for increasing the pH of gastric juice. Cimetidine has been evaluated using various doses with different routes of administration, and the reports often have included comparative studies with anticholinergics as well as antacids. A dosage of 5 mg/kg of body weight, or 300 mg of cimetidine for the adult, has been demonstrated to be effective in increasing gastric pH to more than 2.5 and decreasing gastric volume to less than 0.4 ml/kg of body weight. Intramuscular cimetidine has a peak effect in 15 to 30 minutes and a duration of four to six hours. Cimetidine has few side effects in a single-dose administration. Although mental confusion, headaches, dizziness, diarrhea and soreness at the injection site all have been reported, no adverse reactions have been recognized following a single administration of cimetidine.

In this study, intramuscular administration of 300 mg of cimetidine significantly increased gastric pH and decreased gastric volume to less than one-third of the control value when it preceded induction of anesthesia by one hour.

The time from drug administration to induction of anesthesia ranged from 25 to 75 minutes, with a mean of 59.7 ± 15.6 minutes. The majority of subjects fell within the ideal 30 to 60-minute time interval, which demonstrated the effectiveness of a single intramuscular dose of cimetidine on increasing gastric pH and reducing gastric volume.

Because of the nature of the outpatient surgical setting and occasional reports of hypotension and cardiac dysrhythmias with intravenous cimetidine, the intramuscular route of administration was utilized. A report by Weber has suggested that premedication with oral and intramuscular cimetidine produces a greater and more consistent rise in gastric pH than does oral cimetidine alone. In this study, a single intramuscular administration of cimetidine significantly increased the gastric pH and reduced gastric volume beyond the "safe" side of the critical values proposed for acid aspiration pneumonitis. Cimetidine was well received by all the patients studied, who demonstrated no adverse side effects from a single preoperative administration. Reactions at the injection site were uncommon, and only one patient in 15 complained of transient pain.

Summary

In summary, this study demonstrated that 80% of the control patients were at significant risk of aspiration pneumonitis compared with 26% of Bicitra® and 0% of cimetidine-treated patients. Bicitra® (73%) and cimetidine (100%) both were effective in increasing the gastric pH above the critical level of 2.5. However, 93% of the patients treated with Bicitra®, compared with 6% of the patients treated with cimetidine, had gastric volumes exceeding 0.4 ml/kg of body weight.

A single intramuscular administration of 300 mg of cimetidine 30 to 60 minutes prior to the induction of anesthesia is more effective in elevating gastric pH and reducing gastric volumes in the unpremedicated adult ambulatory surgical patient than is oral Bicitra®. Administration of 15 ml of Bicitra® 15 minutes prior to the induction of anesthesia is effective in increasing gastric pH above the 2.5 level in the majority of patients, minimizing the risk of acid aspiration pneumonitis despite the significant gastric volume. Should cimetidine be contraindicated,
Bicitra® would be an effective adjunct for patients who are considered to be at risk for acid aspiration pneumonitis.

Considering the safety of cimetidine, its minimal side effects with a single preoperative administration and its relatively low cost to the patient compared to the potential dangers of acid aspiration pneumonitis during anesthesia, cimetidine should be considered for routine prophylactic use with high-risk unpremedicated adult ambulatory surgical patients.

REFERENCES


AUTHORS

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