Comparison of oral and intramuscular lorazepam as a surgical premedicant on gastric pH and volume

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Fort Lewis, Washington

The purpose of this study was to determine whether lorazepam or its method of administration had an effect upon the volume and/or the acidity of gastric contents. In addition, the effectiveness of lorazepam was also evaluated.

Utilizing an experimental, randomly assigned and double blind design, 60 adult surgical patients requiring general anesthesia and endotracheal intubation were randomly assigned into one of three groups: Group I received oral and intramuscular placebos; Group II received oral lorazepam and intramuscular placebos; and Group III received oral placebos and intramuscular lorazepam. Pre-treatment and post-treatment measurements of blood pressure, pulse and respirations were recorded. In addition, the effectiveness of lorazepam was evaluated by means of a combination of a patient self-assessment scale and observation techniques. After a standard anesthetic induction and intubation, gastric contents were suctioned. The gastric aspirate was measured in ml and in pH units with a pH meter.

This research concluded that patients receiving lorazepam as a preoperative medication demonstrated an association with decreases in gastric acidity and volume. There were no significant differences detected in pH or volume when the oral route was compared with the intramuscular route. In addition, lorazepam, in both the oral and intramuscular preparations, demonstrated decreases in restlessness and increases in slurred speech.

The administration of medication to patients prior to the onset of anesthesia and surgery is a well documented practice that dates back more than a century. This practice is presently employed by most practitioners in anesthesia.

The goals of premedication vary among individual practitioners and clinical situations. One of the most common goals of premedication is the relief of anxiety. Other goals include alterations of psychological and physiological parameters. In order to achieve some of these effects, there exist numerous drugs and drug classifications which may be administered alone or in combination to produce single, combined or synergistic effects.

Physiologic parameters that concern anesthetists include the quality and quantity of gastric secretions. These secretions are of interest because of an increased potential for pulmonary aspiration during the anesthetic process, possibly resulting in severe pulmonary damage as originally described by Mendelson. Although specific levels are not
known, it is generally accepted that an increase in the acidity and volume of pulmonary aspirate will lead to greater pulmonary insult. This insult may range from a minor and localized atelectasis to a profound morbidity leading to death. Such concerns may influence the choice of a particular premedicant as well as its route of administration.

Lorazepam, an anxiolytic agent of the benzodiazepine family, is an accepted drug for use as a surgical premedicant. To date, published reports are not available with regard to the gastric effects of preoperative lorazepam.

**Materials and methods**

Prior to beginning the study, approval was obtained from appropriate committees at the State University of New York at Buffalo's School of Nursing and the Veterans Administration Medical Center in Buffalo, New York, both of which were affiliated with this research. After detailed explanation of the study and its procedure, all participants signed an informed consent.

This research utilized an experimental, randomly assigned and double blind design. A total of 60 patients were included in the study. There were three groups, each consisting of 20 participants: Group I received oral and intramuscular placebos; Group II received oral lorazepam and intramuscular placebos; and Group III received oral placebos and intramuscular lorazepam.

Patients eligible to participate in the study were adults requiring surgery, general anesthesia and endotracheal intubation. There were numerous exclusion criteria which eliminated patients presenting with any condition that had the potential to alter gastric contents. These criteria included the physical and psychological state of the patient, the nature of the surgical procedure, and/or pharmacologic preparations that the patient may have been receiving.

All patients in the study were required to have routine hematological and chemistry studies. In addition, patients' age, height, weight, vital signs and effectiveness of treatments were recorded.

On the morning of surgery, prior to the administration of medications, control vital signs consisting of blood pressure, pulse and respiratory rate were obtained. After vital signs were obtained, baseline data to determine the effectiveness of premedication was obtained by a method similar to that described by Forrest. This method consisted of the author obtaining the patient's own estimate of his or her degree of sleepiness, apprehension, confusion, restlessness, headache, dizziness, nausea, dry mouth and vomiting. The author then estimated the patient's degree of sweating and slurred speech. These 11 items, each scored on a scale of 0 (none) to 9 (most severe), became the baseline data for examining the effects of the premedication. The 11 variables of this scale were consistently obtained in the same manner and sequence.

Treatments were administered approximately two hours prior to induction. Lorazepam doses for the intramuscular and oral routes were 0.05 mg/kg rounded off to the nearest 0.5 mg. Oral medications and placebos were administered with 30 ml water. Normal saline was utilized for the intramuscular placebo.

Approximately 90 minutes after premedication the patient was transferred to a designated study area in the operating room where blood pressure, pulse, respiratory rate and effectiveness scale were repeated.

All patients received a standard anesthetic induction consisting of fentanyl as indicated, 5 mg tubocurarine, 3.5 mg/kg thiopental, 1-1.5 mg/kg succinylcholine, endotracheal intubation and isoflurane, enflurane or halothane with nitrous oxide and oxygen.

After securing the endotracheal tube, an orogastric tube was inserted into the stomach via the oral cavity. Position was verified by insufflation of 30 ml air and auscultation. Gastric contents were suctioned with the patient in the supine, slight Trendelenburg, modified right and left lateral positions. Immediately after final suction, the gastric tube was removed. Volume was measured in ml with a graduated syringe. Acidity was measured in pH units with an Orion Research Digital Ionalyzer 501. This pH meter was utilized for all determinations and was calibrated on a daily basis by the author.

To ascertain effects of premedication both within and among groups, the data regarding gastric pH was analyzed utilizing a one-way analysis of variance (ANOVA). After differences were detected among groups, planned pairwise comparisons were made. When assumptions for this statistical procedure were violated, as in the case of the volume data, nonparametric tests were utilized. Data relating to the effectiveness scale were analyzed by the Wilcoxon matched-pairs signed-ranks test.

**Results**

To support the assumption of homogeneity between groups prior to testing, numerous statistical procedures were employed on pre-treatment vari-
ables. These analyses revealed no statistically significant difference between groups with respect to laboratory data, vital signs or physical characteristics such as age, height and weight. Descriptive grouped data of pre-treatment variables is contained in Table I.

**Effectiveness scale.** Group I (control group) received the placebo pill and placebo injection. This group demonstrated a statistically significant decrease ($p < 0.01$) in the level of restlessness as perceived by the patient. An attempt to explain this finding may rest in the possibility that the patient actually experienced a placebo effect from the treatment or the patient demonstrated a Hawthorne-like effect. The Hawthorne effect refers to a change in behavior of subjects because of their awareness of their participation in a study. This is a potential threat to both internal and external validity. Minimizing this threat is the presence of a design which includes a placebo group and a double blinded technique. The pre-treatment and post-treatment scores for the remaining 10 variables in Group I did not demonstrate any statistically significant differences.

Group II (oral lorazepam) demonstrated statistically significant differences with three variables. The level of sleepiness, as perceived by the patient, was increased ($p < 0.005$). Restlessness, as perceived by the patient, was decreased ($p < 0.005$). A statistically significant increase was also noted with slurred speech ($p < 0.005$). The remaining eight variables of Group II did not demonstrate any significant differences.

Group III (intramuscular lorazepam) demonstrated statistically significant differences with two variables. The level of sleepiness, as perceived by the patient, was increased ($p < 0.005$). The level of slurred speech, as evaluated by the author, was significantly increased ($p < 0.005$). The remaining nine variables of Group III did not demonstrate any significant differences. It is of interest to note that none of the groups reported changes or decreases with regard to their levels of anxiety. This latter finding was consistent with the findings of Forrest, who was also unable to demonstrate a significant effect upon the reduction of patients’ preoperative anxiety when six intramuscular premedicants were analyzed.

The significant grouped data results for effectiveness of the treatments is presented in Table II.

**pH and volume data analysis.** After the gastric aliquot was obtained it was measured for acidity in pH units. A summary of the mean pH data is presented in Figure 1. An ANOVA of this data with planned comparisons demonstrated a statistically significant difference ($p = 0.01$) in pH values when either the intramuscular or the oral route was compared to placebo. This ANOVA failed to demon-

### Table I
Descriptive data of age, height, weight and pre-treatment vital signs

<table>
<thead>
<tr>
<th>Group</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>56</td>
<td>51</td>
<td>61</td>
</tr>
<tr>
<td>Mean heights (inches)</td>
<td>70</td>
<td>70</td>
<td>69</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>86</td>
<td>77</td>
<td>79</td>
</tr>
<tr>
<td>Pre-treatment pulse (bpm)</td>
<td>74</td>
<td>72</td>
<td>79</td>
</tr>
<tr>
<td>Pre-treatment respirations (bpm)</td>
<td>18</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Pre-treatment systolic (mmHg)</td>
<td>128</td>
<td>127</td>
<td>127</td>
</tr>
<tr>
<td>Pre-treatment diastolic (mmHg)</td>
<td>80</td>
<td>80</td>
<td>77</td>
</tr>
</tbody>
</table>

### Table II
Significant results, effectiveness scale

<table>
<thead>
<tr>
<th>Group</th>
<th>Method</th>
<th>Effect</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>(Control)</td>
<td>Restlessness</td>
<td>↓ (p &lt; 0.01)</td>
</tr>
<tr>
<td>Group II</td>
<td>(PO)</td>
<td>Sleepiness</td>
<td>↑ (p &lt; 0.005)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Restlessness</td>
<td>↓ (p &lt; 0.005)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slurred speech</td>
<td>↑ (p &lt; 0.005)</td>
</tr>
<tr>
<td>Group III</td>
<td>(IM)</td>
<td>Sleepiness</td>
<td>↑ (p &lt; 0.005)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slurred speech</td>
<td>↑ (p &lt; 0.005)</td>
</tr>
</tbody>
</table>
strate a significant difference between the oral and intramuscular groups with respect to their effect upon gastric pH.

Immediately after the gastric fluid aliquot was obtained, it was measured in ml. A summary of the mean volume data is presented in Figure 2. A Kruskal-Wallis ANOVA demonstrated an association of decreased gastric volume ($p = 0.066$) when lorazepam was administered either orally or intramuscularly. There was no difference detected between the oral and intramuscular groups with respect to their effect upon gastric volume.

The descriptive grouped data of gastric pH and volume is contained in Table III.

**Discussion**

**Conclusions.** It is concluded that patients receiving lorazepam demonstrated an association with decreases in gastric acidity and gastric volume when compared to placebos. Furthermore, it is concluded that the oral administration of lorazepam as a premedicant does not increase gastric volume when compared to intramuscular lorazepam. In effect, this should decrease the potential for pulmonary damage should aspiration occur. These conclusions parallel those of Hjortso and Mondorf\textsuperscript{10} who compared intramuscular and oral diazepam and their effects upon gastric pH and volume. The findings of this study also support the conclusions of Murie and MacKay,\textsuperscript{11} who demonstrated that pentagastrin-stimulated gastric secretion was significantly reduced in patients pretreated with lorazepam.

**Implications for practice.** Seventy five percent (15/20) of the patients in the control group had gastric pH values less than two. This value is considered to be an extremely dangerous level that has the potential for severe pulmonary damage should aspiration occur. The percentage of low gastric pH values experienced in this control group is consistent with other control groups in similar studies. These findings may suggest a rethinking with respect to the pharmacological preparation of patients about to undergo anesthesia and surgery.

Presently, in the author's institution, virtually...
all patients presenting for anesthesia and surgery are pharmacologically premedicated with oral ranitidine. This H₂ receptor antagonist is administered prophylactically to minimize the extent of pulmonary insult should aspiration occur.

Because of its long half-life (15 hours), lorazepam may not be an appropriate choice for patients receiving outpatient anesthesia. Lorazepam may be more appropriately utilized in patients undergoing lengthy procedures and/or patients whose postoperative plans include mechanical ventilation.

**Recommendations for further research.** Patients frequently receive premedicant injections which may be uncomfortable and at times painful. The rationale as to why patients receive intramuscular premedicants is not always clear. Further research with regard to the concepts of the efficacy and safety of oral premedicants should be investigated.

Finally, most patients arrive in the surgical suite with dangerously high gastric acid levels. Worth considering is the question of whether anesthetists should pharmacologically treat more or even all patients in order to reduce their gastric acidity. In addition, since a controlled preoperative environment is not present in outpatient anesthesia, an investigation examining whether anesthetists should pharmacologically treat these patients to alter their gastric contents might be valuable.

**REFERENCES**


AUTHOR

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The opinions or assertions presented in this article are those of the author and are not to be construed as official or as reflecting the views of the Department of Defense or the United States Army.
1. Most drugs are weak acids or weak bases; consequently, they are in equilibrium between their charged and uncharged forms. Because the passage of uncharged molecules through a membrane lessens their number, the equilibrium responds to this stress of a change in concentration by shifting so there is more of the uncharged form available. A charged portion is needed to dissolve in the circulating blood, ECF and ICF.

2. This patient has chronic respiratory acidosis that is compensated as expected with an increase in the HCO₃⁻ of 4 meq/L for every 10 mmHg increase in the PCO₂. The oxygen content is satisfactory. No effort should be made to lower the PCO₂ during the anesthesia.

3. The K⁺ needs to be checked. A deficit caused by the diuretic may be contributing to, or causing, her metabolic alkalosis, or decrease in H⁺. If there is hypokalemia, after satisfactory replacement of K⁺, the H⁺ should also increase. Surgery probably may take place. Because of the edema mentioned so briefly, it must be assumed that there are other problems. The increased PCO₂ is as expected and is the “normal” as long as the HCO₃⁻ is elevated as described. It should not be reduced as long as the PO₂ remains satisfactory.

4. The metabolic compensation is as expected for acute respiratory alkalosis. When his pain is relieved his acid/base condition will be normal.

5. This patient has a chronic respiratory alkalosis. The psychoneurotic patient can hyperventilate chronically. The metabolic compensation is as expected, that is there is an approximate 4 meq/L decrease in the HCO₃⁻ for every 10 mmHg decrease in the PCO₂. If the practitioner allows the PCO₂ to increase to 40 mmHg pressure under anesthesia, the bicarbonate will increase the 1 meq/L that occurs in the acute acidic respiratory change and the HCO₃⁻ will be 21 meq/L. The pH will then be 7.34, very slightly acidotic, as compared to the former 7.45 which is very slightly alkalotic. This patient is used to this latter internal environment and to change her temporarily is undesirable.
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