Evaluation of the Efficacy of Alka-Seltzer Effervescent in Gastric Acid Neutralization

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A commercially available antacid, a mixture of sodium and potassium bicarbonates and citric acid (Alka-Seltzer Effervescent), was evaluated experimentally and clinically for its efficacy in neutralizing 0.1 N HCl and gastric contents. In an in vitro titration study, Alka-Seltzer Effervescent buffered 5–30 times the volume of HCl with a pH between 1.0 and 2.0 to above a pH of 2.5. In an isolated canine pulmonary lobe model, aspiration of the antacid or acid–antacid mixture caused only a mild increase in lobe weight and did not increase intrapulmonary shunting. In the clinical study, when the antacid was given 5–40 min before administration of general anesthesia in a group of patients for emergency surgery, the pH of the gastric contents in each patient was increased to above 4.0. This contrasts with the control group of patients, which showed 50% ($P < 0.05$) of the patients were at risk when no antacid was administered. Preoperative administration of Alka-Seltzer effectively increases the pH of the gastric contents in patients undergoing emergency surgery.

Key Words: GASTROINTESTINAL TRACT—antacids. LUNG—aspiration. COMPLICATIONS—aspiration.

The risk of aspiration during general anesthesia has been recognized for over one hundred years (1). For the past two decades, attempts have been made to reduce gastric acid using pharmacological agents, with varying success (2–6). The varying success is in part due to poor mixing between the gastric contents and the antacids (7,8). This is particularly true for emulsion (particulate) forms of antacids. It is, therefore, generally agreed that aqueous forms of antacids are superior to emulsion forms. Currently, sodium citrate in an aqueous form is most frequently employed (5,6). However, it is not commercially available and special preparation of the agent is necessary. Because there are no universally accepted regimens or pharmacological compounds that are ideal for all clinical situations, we have evaluated the efficacy of a commercial mixture of sodium and potassium bicarbonates and citric acid (Alka-Seltzer Effervescent) in reducing gastric acidity both experimentally and clinically.

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Materials and Methods

In Vitro Study

Experiments were done at room temperature. Two tablets of Alka-Seltzer Effervescent dissolved in 30 ml of distilled water (pH = 6.8) were added in 0.5-ml increments to 30-ml samples of hydrochloric acid with a pH of 1.0, 1.2, 1.5, 1.8, and 2.0. Changes in pH were measured using a Corning model 10 pH meter.

Animal Study

Experimental Preparation. An isolated, ex vivo, perfused, ventilated canine pulmonary lobe preparation was used as described previously (9). Under pentobarbital (30 mg/kg) anesthesia, the left lower pulmonary lobe was isolated through a lateral thoractomy. The pulmonary vein, artery, and bronchus were cannulated and the lobe was removed. The lobe was suspended in a heat and humidity controlled chamber from a weight transducer with the hilar structures in a dependent position. The lobe was ventilated with a Harvard piston type ventilator at a rate of 10 breaths/min using 100% oxygen. Tidal volume was approximately 2 ml/g of lobe weight. The perfusate consisted of 800 ml of heparinized autologous blood.

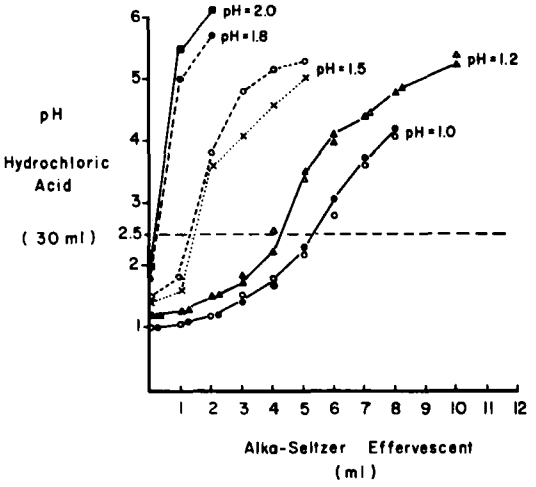

Figure 1. In vitro titration curves: volumes of the antacid solution required to increase pH to above 2.5 of solutions of HCl with pH 1.0–2.0.

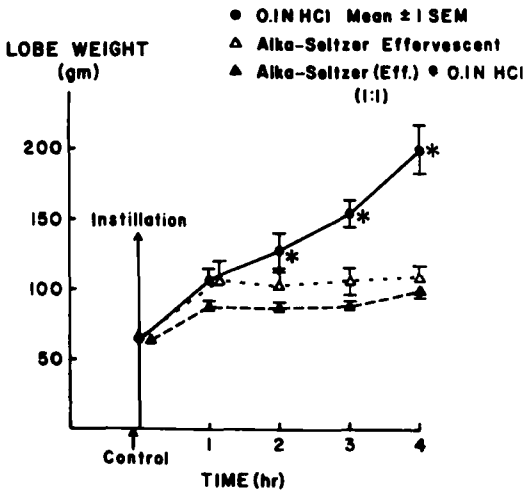

Figure 2. Changes in lobe weight (mean ± SEM) after aspiration of hydrochloric acid, antacid, and acid–antacid mixture. *$P < 0.05$ for difference between the groups.

Pulmonary venous drainage (oxygenated) was collected in a reservoir and then passed through a Bentley infant oxygenator. A gas mixture of 95% nitrogen and 5% carbon dioxide was used to deoxygenate the pulmonary venous (oxygenated) blood, which then was perfused into pulmonary artery by a Sarns roller pump. The flow rate was increased slowly until the pulmonary arterial pressure reached 15 mm Hg. Thereafter, blood flow was kept constant. The flow generally was in the range of 2 ml/g of lobe weight per min. Venous pressure was kept at 0 to −2 cm of water relative to the hilum. Temperature of the autologous perfusate was maintained at 38 ± 1°C. Pulmonary arterial, venous, and peak inspiratory pressures and lobe weight were monitored continuously with transducers and recorded periodically with a multiple-channel recorder. Arterial and venous blood samples were analyzed periodically for pH, P_{CO_2}, and P_{O_2} with a blood-gas analyzer. Sodium bicarbonate was added to perfusate as needed to maintain normal acid–base balance. Pulmonary arterial blood samples were used for hemoglobin determination.

Experimental Protocol. All lobes were perfused for 30 min to allow them to stabilize, and then were placed into one of the following groups. The commercial antacid solution was prepared by dissolving two tablets of Alka-Seltzer Effervescent in 30 ml distilled water.

GROUP I. HYDROCHLORIC ACID (5 LOBES). After stabilization, 0.2 ml of 0.1 N hydrochloric acid (pH 1.0) per gram of lobe weight was instilled into the bronchus. Measurements described above were made for 4 hr. Samples of arterial and venous blood were drawn at 30-min intervals for calculation of shunt.

GROUP II. HYDROCHLORIC ACID–ANTACID MIXTURE (5 LOBES). After stabilization, 0.2 ml of a mixture of equal volumes of 0.1 N hydrochloric acid and commercial antacid solution (pH 5.4) per gram of lobe weight was instilled into the bronchus. The preparations were monitored as in group I.

GROUP III. ANTACID SOLUTION (5 LOBES). After stabilization, 0.2 ml of the commercial antacid solution (pH 6.8) per gram of lobe weight was instilled into the bronchus. The preparations were monitored as in group I. Intrapulmonary shunt was calculated with the standard shunt formula and all results were subjected to statistical analysis by the Student's *t*-test.

Clinical Study

Eighty patients between the ages of 10 and 71 yr admitted for emergency surgery were studied. The protocol was approved by the Human Studies Committee. The majority of the patients were trauma victims. The period of time between the last oral intake and the induction of anesthesia was 1–8 hr. Patients were alternately assigned to one of two groups.

Group A. Forty patients served as control. No antacid was given before induction of anesthesia. After preoxygenation for 3–5 min, general anesthesia was induced with a rapid-sequence technique. As soon as the endotracheal tube was secured, an 18-F Salem sump nasogastric tube was inserted. Gastric contents were thoroughly aspirated and the pH and volume determined.

Group B. Forty patients were included in the study group. Patients were given 30 ml of a commercial

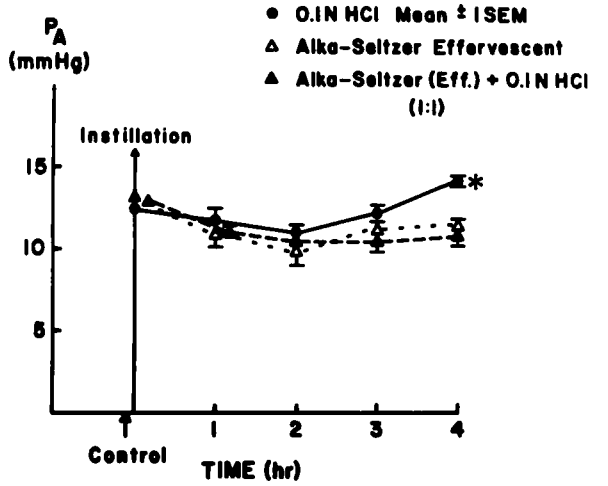

Figure 3. Changes in pulmonary arterial pressures (P_a) (mean ± SEM) after aspiration of hydrochloric acid, antacid, and acid–antacid mixture. *$P < 0.05$ for difference between the groups.

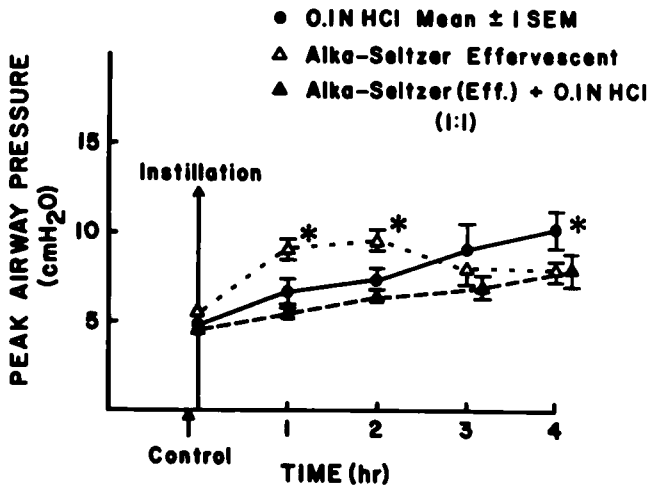

Figure 4. Changes in airway pressure (Paw) (mean ± SEM) after aspiration of hydrochloric acid, antacid, and acid–antacid mixture. *$P < 0.05$ for difference between the groups.

antacid solution, (two tablets of Alka-Seltzer Effervescent dissolved in 30 ml of water) orally 5–40 minutes before induction of general anesthesia. After a rapid-sequence induction of anesthesia as in group A, a Salem sump nasogastric tube was inserted, gastric contents were aspirated, and the pH and volume determined. The data was analyzed with the χ^2 test.

Results

In Vitro Study

The titration curves and antacid dose responses are shown in Figure 1. The in vitro titration study revealed that the commercial antacid solution can buffer from 5–30 times the volume of hydrochloric acid with a pH between 1.0 and 2.0 to a pH above 2.5.

Animal Study

After acid instillation into the bronchus (group I), lobe weight increased 208% (Fig. 2), mean pulmonary arterial (Fig. 3) and mean peak inspiratory pressures (Fig. 4) increased, and intrapulmonary shunting increased 39% (Fig. 5). The lobes became grossly hemorrhagic with areas of focal necrosis. By the end of 4 hr of perfusion, pink frothy edema fluid was issuing from the bronchial airway. Microscopically, the lung showed marked edema and hemorrhage in the alveolar walls. After instillation of the commercial antacid solution into the bronchus (group III), lobe weight increased 60% during the first hour, and thereafter remained stable. Pulmonary arterial and peak inspiratory pressures did not change. There was no increase in intrapulmonary shunting. The lobes appeared normal. Microscopically, only slight to moderate alveolar wall edema was present. When the hydrochloric acid–antacid mixture (group II) was instilled into the lobe, mean lobe weight increased 53% during the 4-hr perfusion. Mean pulmonary arterial and mean peak inspiratory pressures were stable and no intrapulmonary shunting developed (Figs. 2–5). The lobes appeared normal. Microscopically, only slight to moderate alveolar wall edema and areas of minimal focal hemorrhage were seen.

Clinical Study

Age, sex, mean weight, and duration of fasting in the two groups were similar.

Group A. The volume of gastric juice contents varied from 15–800 ml with a mean of 69.5 ± 19.8 ml (mean ± SEM). Sixty-five % (26 patients) of the patients had gastric volumes greater than 25 ml. The pH of the gastric juice ranged from 1.0–4.5. Sixty % of the patients had a gastric pH ranging between 1.5–2.0, and 20% between 1.0–1.5. In 80% of the patients (32 patients), gastric pH was lower than 2.5. Fifty percent of the patients had both a gastric pH of less than 2.5 and a gastric volume greater than 25 ml.

Group B. The volumes of gastric contents ranged from 10–600 ml with a mean of 65.4 ± 15.6 ml (mean ± SEM). This is not significantly different from control group ($P > 0.1$). In all 40 patients, the pH of gastric juice was greater than 4.0 (4.0–6.5). This difference is statistically significant from control group ($P < 0.05$).

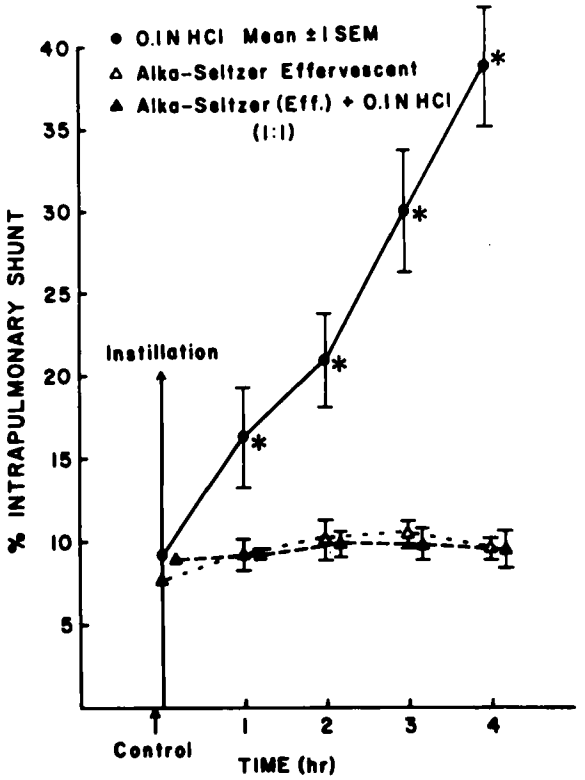

Figure 5. Changes in the intrapulmonary shunting (mean ± SEM) after aspiration of hydrochloric acid, antacid, and acid–antacid mixture. *$P < 0.05$ for difference between the groups.

Discussion

Aspiration pneumonitis occurs when acid gastric contents come in contact with respiratory epithelium. This is most likely to occur during induction of anesthesia in patients with a full stomach, because normal protective airway mechanisms are lost. The critical risk factors have been shown to be aspiration of a volume greater than 25 ml with a pH less than 2.5 (3).

In theory, gastric acidity can be reduced locally by antacids, or centrally by inhibiting acid secretion. Cimetidine, an H_2-antagonist, has been shown to be effective in reducing both gastric juice and gastric acid (10–12) and also to be superior to antacids (13). However, it has the disadvantage of requiring a period of several hours after reaching effective blood levels to exert its inhibitory effect. Cimetidine also does not neutralize acid already in the stomach. In an emergency situation, both theoretically and practically, cimetidine cannot be relied upon (14).

Although the idea of neutralizing gastric acid before induction of general anesthesia was originally suggested by Mendelson in 1946 (15), it was not until two decades later that a study appeared reporting prophylactic antacids given in emergency situations (2). Antacids such as magnesium trisilicate mixture (BPC), Maalox, and Mylanta have been employed, but were abandoned because of lung damage that resulted from aspiration of the antacid, damage which was thought to be due to the particulate nature of the preparation (16) or to poor mixing of the agent with gastric juice (7,8). Because of this, many have suggested that a clear liquid soluble antacid would be more desirable. Currently, sodium citrate is the agent chosen by most anesthesiologists (5,6). It has recently been shown to be harmless when introduced into the lung (17).

The isolated ex vivo canine pulmonary lobe preparation has been utilized extensively for the study of hydrochloric acid aspiration (9,18). The model is stable, and the injury reproducible. With pulmonary perfusion and ventilation kept constant, pulmonary injury can be studied without being influenced by systemic responses. In this study, the model was utilized to evaluate the effectiveness and safety of an aqueous citrate antacid, Alka-Seltzer Effervescent, in preventing pulmonary injury.

Alka-Seltzer Effervescent consists of sodium and potassium bicarbonates and citric acid in a dry tablet. It is converted mainly to sodium citrate when dissolved in water. In many respects, this solution is similar to 0.3 M sodium citrate solution. In our in vitro studies, Alka-Selzter Effervescent antacid solution (two tablets in 30 ml water) was capable of buffering 5–30 times the volume of hydrochloric acid solutions with a pH between 1.0–2.0 to above the critical level of 2.5 (Fig. 1). In the animal study, we evaluated the extent of the pulmonary injury caused by both hydrochloric acid and Alka-Seltzer Effervescent alone, and a mixture of the two agents. When acid alone was instilled, increases in lobe weight were massive, and a marked increase in intrapulmonary shunt occurred. When antacid alone was instilled, the increase in lobe weight was moderate and there was no increase in intrapulmonary shunt. When the acid–antacid mixture was instilled, increases in lobe weight were minimal and there was no increase in intrapulmonary shunt. Both solutions, the antacid and the acid–antacid mixture, are hyperosmolar (1440 and 740 mOsm/L, respectively) and, because both have a pH above the critical level of 2.5 (pH 6.8 and 5.4, respectively), it is likely that the increase in lobe weights seen in the two groups was caused by the osmolarity of the solutions. It is possible that when the solutions were instilled, fluid was drawn into the alveolar space and this caused the minimal to moderate increases in lobe weight.

The clinical trial demonstrated that Alka-Seltzer Effervescent solution given orally 5–40 min before the induction of anesthesia effectively elevated the gastric

juice pH above the critical level of 2.5 without increasing volume of gastric contents. If one uses a volume greater than 25 ml and a pH less than 2.5 as criteria for the risk of developing aspiration pneumonia, none of the patients given Alka-Seltzer Effervescent were at risk, even though in some patients the antacid solution was given orally a few minutes before induction. It has been shown by Gibbs et al. (6) and Viegas et al. (19) that the effect of sodium citrate given orally before surgery lasted from 60–180 min. Because the active ingredient of the Alka-Seltzer Effervescent solution is sodium citrate, a similar duration of effect could be expected. One patient in the control group had a gastric volume content of 800 ml. In this patient, 30 ml of the antacid solution would not have sufficiently buffered the contents to a pH above the critical level of 2.5, if the original pH was 1.2 or lower. However, because in the majority of the patients the pH of the gastric content was between 1.5 and 2.0, and the gastric volume considerably less than 800 ml, 30 ml of Alka-Seltzer Effervescent solution should be sufficient to elevate the pH to above 2.5.

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