

## Comparison of Intravenous Ranitidine with Pantoprazole in Decreasing Gastric Fluid Acidity in Emergency Cesarean Section

Alipour M<sup>1</sup>, Soltani Gh<sup>2</sup>, Zirak N<sup>2</sup>, Paravi Torghabeh N<sup>3</sup>, Peivandi Yazdi A<sup>4\*</sup>

<sup>1</sup>. Assistant professor of Anesthesiology, Cardiac Anesthesia Research Center, Faculty of medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

<sup>2</sup>. Associated professor of Anesthesiology, Cardiac Anesthesia Research Center, Faculty of medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

<sup>3</sup>. Assistant of Anesthesiology, Cardiac Anesthesia Research Center, Faculty of medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

<sup>4</sup>. Assistant professor of Anesthesiology, Research Center for Patient Safety, Mashhad University of Medical Sciences, Mashhad, Iran.

ARTICLE INFO	ABSTRACT
<p><i>Article type:</i> Original Article</p> <hr/> <p><i>Article history:</i> Received: 30- Aug-2013 Accepted: 20- Sep-2013</p> <hr/> <p><i>Keywords:</i> Caesarian section Pantoprazole Pulmonary aspiration Ranitidine</p>	<p><b>Objectives:</b> Peri-operative aspiration of gastric contents is a problem that causes certain respiratory problems including ARDS. Prophylaxis against aspiration of gastric contents is performed routinely in elective surgeries, but there is rare evidence on the efficacy of this method in emergency cesarean section.</p> <p><b>Materials and Methods:</b> This is a randomized, controlled, double-blinded clinical trial. 60 parturients undergoing emergency cesarean section were randomly assigned into three groups of 20 each. They were allocated into two study and one placebo groups. The study group one and two received intravenous ranitidine (IV) 50 mg or IV pantoprazole 40 mg, half an hour before induction of GA, respectively. The placebo group was administered just 5 ml of isotonic saline half an hour before GA induction. After intubation and confirmation of endotracheal tube insertion, the gastric contents were aspirated through a nasogastric tube for evaluation of acidity and volume.</p> <p><b>Results:</b> A statistical difference between group one and two with the control group was observed in the acidity of gastric contents, but there was no difference in volume. Also, the PH level of gastric contents in patients receiving pantoprazole was significantly higher than the isotonic saline (<math>p &lt; 0.001</math>) and ranitidine groups. The difference in average level of acidity of gastric contents in patients receiving pantoprazole and ranitidine showed a marginal significance (<math>p \leq 0.036</math>).</p> <p><b>Conclusion:</b> Our findings revealed that pre-operative administration of H<sub>2</sub>-blockers and proton pump inhibitors (PPIs) effectively decrease the acidity of gastric contents even in emergency cesarean sections. In addition, if the data had an isotonic distribution, or if there were a large number of cases in different clinical groups, PPIs could possibly be more effective.</p>

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### Introduction

Application of muscle relaxants for facilitating tracheal intubation makes the patients prone to

pulmonary aspiration of gastric content. Several methods have been used to inhibit this event; however, each of them has their own limitations and deficiencies. Non-per oral (NPO) ordering

\* Corresponding Author: Email: peivandia@mums.ac.ir, Tel: +985118525209

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can be singled out as the first protective method which allows for gastric emptying before anesthesia induction. The required time for gastric emptying would vary, depending on the kind of food or drink and the underlying condition affecting the gastric emptying process. It is obvious that this method cannot be used in most emergency operations, in which there is not enough time for gastric emptying. And in fact, emergency operations as well as Caesarean sections are considered as a limitation of this method.

The next method which is likely to be used in emergency operations, is the rapid sequence induction (RSI) method which reduces the time span between the administration of muscle relaxants, intubation and inflation of the tracheal tube cuff and can work through the use of muscle relaxants with a rapid onset of action, such as succinylcholine.

However, it should be noted that the above mentioned methods are not fully protective and despite the use of Cricoid pressure on the cartilage, there is still the possibility of pulmonary aspiration (1).

The existence of the above-mentioned limitations on one hand, and the costs and side effects of pulmonary aspiration imposed on the patients on the other, have brought about a large number of studies in order to reduce the side effects of pulmonary aspiration. Among those, the methods based on reducing the acidity and minimizing the gastric content can be singled out as effective.

For emergence of the clinical symptoms of aspiration pneumonia, there must be a minimum gastric content of 20 ml and a PH of less than 2.5 so that the primary damage, which is in fact a chemical burn, is produced (2).

The appearance of primary pulmonary aspiration under certain circumstances can lead to secondary bacterial pneumonia or more severe side effects. Based on this, it is strongly recommended to prescribe proper medications or administer any possible method to reduce the volume of gastric content besides increasing its PH.

With due respect to the side effects and high costs of post-operation pulmonary aspiration which threaten healthcare systems, due to long-term hospitalization in the ICU, it seems that taking measures which reduce the possibility of pulmonary aspiration is the easiest and most cost-beneficial approach (3).

Several studies have been carried out in this regard. Each of them tried to examine the case

from a different viewpoint. In elective operations in which there is enough time, the best method is to go through the NPO phase and let the stomach become empty during a natural process. Depending on the specifications of the patient and type of the food intake, a time range of two hours (for skimmed liquids) to 8-12 hours (in the case of diabetic gastroparesis and partial blockings) has been recommended.

Moreover, the administration of H<sub>2</sub> blockers during the night before the operation and early on the operation day has evident positive impact on preventing the occurrence of pulmonary injuries in the case of possible pulmonary aspiration (4).

So far, in related studies, in such operations and particularly in C-sections, numerous methods have been investigated out of which neither have provided a 100% protection against aspiration; however, they are capable to reduce its possibility.

Among the common methods applicable during C-section, rapid induction and tracheal intubation anesthesia can be singled out as effective. However, in spite of observing all safety cautions and exerting pressure on the Cricoid cartilage, there is a chance that aspiration happens once the food returns to the oropharyngeal space. The Sellick maneuver does not have any protective role against micro-aspirations.

Accordingly, further studies were carried out with the purpose of changing the composition of the gastric contents which have an explicit effect on the injury. They managed to reduce the degree of the primary chemical injuries by increasing PH and reducing the bulk of gastric content.

Likewise, H<sub>2</sub> blockers and PPI, non-particle antacid medications are of high importance in the management of this problem. Usually, due to the emergent nature of such operations, the time interval between decision making and operation is less than an hour. Thus, these medications can work efficiently and reduce the side effects of pulmonary aspiration to a great extent (5).

The general objective of this study was to evaluate the impact of I.V. ranitidine and pantoprazole along with placebo in reducing the acidity of gastric contents in patients undergoing C-section.

## Materials and Methods

This is a randomized, double blind clinical trial which its protocols were approved by Mashhad University Ethics committee as a student thesis. The target group in this study included 60 pregnant women who underwent an emergency

Caesarean section operation in Ghaem Hospital, Mashhad, Iran. Patients were informed about the study protocol and possible risks prior to entrance. They were divided randomly into three groups: 20 patients in the placebo group (received 5 milliliter isotonic saline half an hour before GA induction) and two control groups (either 50 mg IV ranitidine or 40 mg IV pantoprazole half an hour before GA induction). The exclusion criteria were: fetus sufferance for which measurement could not be applied, known dyspepsia problems, and cases under long term treatment with either H2 blockers or Proton Pump Inhibitors (PPIs).

Once the C-section patients were chosen, following GA induction, an adult nasogastric tube was inserted for aspiration of all gastric contents in order to measure the PH level and its volume through gasometrical tools, the Sartorius model. Its measuring accuracy was  $\pm 0.01$ .

The three groups were compared with each other through the use of ANOVA and multiple comparisons. Isotonicization of the gasometric data was verified through the use of Kolmogorov-Smirnov test. The results of this test illustrated an isotonic distribution in the level of gastric content acidity among patients admitted for C-section operation. Kruskal-Wallis test was applied to compare the average data.

## Results

The minimum and maximum age of the patients was 24 and 37 years, respectively, with the average age of  $28.4 \pm 2.81$  years. The average age of patients in the first group receiving isotonic saline was  $28.40 \pm 3.60$  yrs. The patients in the second (ranitidine) and third (pantoprazole) group had an average age of  $28.45 \pm 1.96$  and  $28.65 \pm 2.76$  yrs, respectively. The difference in patients' age was not statistically significant between the three groups ( $p = 0.958$ ).

The mean acidity level of the gastric contents of patients was  $3.37 \pm 0.57$ . It was  $2.68 \pm 0.23$ ,  $3.62 \pm 0.35$  and  $3.81 \pm 0.24$  in patients receiving isotonic saline, ranitidine and pantoprazole, respectively.

The results of the present study revealed that there is a significant difference between the acidity of gastric contents of patients receiving isotonic saline with the ranitidine and pantoprazole groups. The average level of PH of gastric contents in patients receiving isotonic saline was significantly less than that of the patients receiving ranitidine and pantoprazole ( $p < 0.001$ ). The PH level of gastric contents of patients receiving ranitidine was more than the isotonic saline and less than the pantoprazole

groups ( $p < 0.001$ ). Similarly, the PH level of gastric contents in patients receiving pantoprazole was significantly higher than the isotonic saline and ranitidine groups ( $p < 0.001$ ). However, if t-test could be applied to the patients, (if the data had an isotonic distribution, or if there was a large number of cases in different clinical groups), the difference in the average level of acidity of gastric contents in patients receiving pantoprazole and ranitidine showed a marginal significance ( $p \leq 0.036$ ).

There was no difference in the volume of gastric content between the three groups.

## Discussion

In emergent C-section, there is at most one hour time between preparation for the operation and induction of anesthesia. In the present study, the pregnant women were randomly divided into three groups in which they were immediately administered with isotonic saline, ranitidine and pantoprazole, following the decision making of performing C-section by the physician. After the induction of anesthesia and collection the gastric content by a nasogastric tube, which was evenly done in all three groups; the acidity tests showed that in spite of the short time span between the administration of medicine and the preparation of samples, both ranitidine and pantoprazole were significantly effective in reducing the acidity. Also in comparison to isotonic saline, the Sartorius- measured PH was significantly higher in the two other groups. However, regarding the reduction of acidity by ranitidine and pantoprazole, no significant difference was observed. Still, for further comparison of ranitidine and pantoprazole with each other, a wider range of scope and a larger number of cases is required.

A study was carried out by Memis D. in 2003 on 90 patients, all of whom had American society of anesthesiology (ASA) II class and were candidates for elective operations. In this study, the patients were divided into three groups ( $n = 30$ ) and each of the 3 groups received either 5 ml isotonic saline, 50 mg ranitidine or 40 ml pantoprazole, one hour before the operation. After inducing anesthesia, a nasogastric tube was inserted; the gastric content was aspirated and its volume and PH were examined. The average PH in the three isotonic saline, pantoprazole and ranitidine groups, were  $3.73 \pm 0.82$ ,  $5.30 \pm 1.84$  and  $4.8 \pm 1.40$ , respectively whereas no significant statistical difference between the second and third group was found (6).

However, there was a significant difference between group 1 and the two other groups (2 and 3). The gastric content volume of the two ranitidine and pantoprazole groups was significantly lower than that of the isotonic saline group. Consequently, administration of IV pantoprazole and ranitidine, one hour before the operation was selected as the effective means for reducing the acidity and gastric content (7).

In another study in 1993, carried out in South Africa, emergency C-section candidates were immediately administered with 30 ml of sodium citrate and divided into two groups. The first group received 5 ml IV isotonic saline and the second group received 50 mg IV ranitidine. After standard induction of anesthesia through a nasogastric tube insertion, the gastric content was suctioned and its PH level was examined. In this study, the patients with a PH level of less than 3.5 ( $\text{PH} \leq 3.5$ ) and volume of more than 25 ml were considered in the threat of pulmonary injuries. It was observed that 5.6 % of patients in the sodium citrate group, versus 3% of those in the ranitidine plus isotonic saline group were exposed to danger, which means that ranitidine was significantly effective (8).

In a different study in 2008, 80 pregnant women who were candidate for C-section operation were included and divided into 4 groups of 20 patients each. 5 ml of isotonic saline, 10 mg of metoclopramide, 50 mg ranitidine and 40 mg pantoprazole were administered intravenously an hour before the induction of anesthesia to each group, respectively. All groups were under standard induction of anesthesia and after inflating the cuff by the nasogastric tubes; the contents were aspirated and examined. The results were as follows: 12 (60%) patients in group one had a content level of more than 25 ml, while 18 (90%) patients had a PH of less than 2.5 (9).

These studies revealed that in specific operations such as C-section in which there is not enough time before the operation begins administration of H2 blockers or proton pump inhibitors during the one hour prior to operation could be highly beneficial.

## Conclusion

Based on the available literature and with regards to the fact that the incidence of airway edema is higher in pregnant women; our findings revealed a 10 times higher possibility of inadvertent esophagus intubation in such patients.

On the other hand, one of the side effects of pulmonary aspiration is the expression of ARDS syndrome. In the best case scenario and at the most-equipped centers, it takes at least six weeks for the lungs to recover from this syndrome to their previous condition. It also takes two years for the patients to return to isotonic life. Thus, if the acidity level and gastric content volume threaten peri-operative pulmonary aspiration, it is highly recommended to take measures in order to lower the acidity and volume of the gastric content, before the induction of anesthesia.

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