Esomeprazole as a prophylactic agent for acid aspiration syndrome in adult patients undergoing elective surgery: A triple blind placebo controlled clinical trial

Hussein A, Al-Saeed AH, Habib SS

Department of Anaesthesiology, King Khalid University Hospital, Al-Riyadh, Saudi Arabia
College of Medicine and King Saud University Hospitals, King Saud University, Saudi Arabia
Department of Physiology, King Saud University, Saudi Arabia

Correspondence to: Dr A Hussein, e-mail: draaltaf@yahoo.com

ABSTRACT

Background: To explore the effect of single oral dose of esomeprazole 20 mg, administered a night before surgery, on intragastric pH and volume in adult patients undergoing elective surgery by excluding cases contaminated with duodenogastric refluxate.

Patients and Methods: This prospective, triple blind, randomised and placebo controlled clinical trial was conducted to explore the effect of single oral dose of esomeprazole 20 mg, administered a night before surgery, on intragastric pH and volume on 120 adult inpatients of either sex, American Society of Anaesthesiologist physical status I-II, and aged 15–70 years. The patients in Group C (control) received placebo while Group E (Esomeprazole) received esomeprazole orally at 9:00 pm, the night before elective surgery.

On the day of surgery, the gastric contents were aspirated with a large bore, multi-orifice gastric tube passed through an endotracheal tube placed blindly in the oesophagus after tracheal intubation and analysed for pH, volume and the presence of bile salts.

Results: Thirty nine samples (33%) out of 117 were contaminated with duodenal contents. Duodenogastric reflux significantly affected pH and volume in Group C (p value 0.0003 and 0.0016) and E (p value 0.0401 and < 0.0001). Esomeprazole, after excluding samples contaminated with duodenal fluid, significantly increased pH (p <0.0001), decreased volume (p 0.008) and the percentage of the patients (2.56% versus 30.76%) considered “at risk” compared with placebo (p 0.0015) according to the criteria defined (pH $\leq 2.5$ and volume $\geq 25$ ml).

Conclusion: Esomeprazole 20 mg administered orally a night before elective surgery improved the gastric environment (pH $< 2.5$ and volume $> 25$ ml/kg) at the time of induction of anaesthesia excluding samples contaminated with duodenogastric reflux.

Introduction

Duodenogastric reflux is the retrograde flow of duodenal contents into the stomach that then mixes with acid and pepsin. Hughes et al. reported 33%, Raved et al. 8.98% and Wolverson et al. 40% incidence of duodenogastric reflux in healthy subjects. Our first aim was to determine whether or not duodenogastric reflux significantly affects gastric pH and volume.

Esomeprazole, a proton pump inhibitor, is used in peptic ulcers and other acid dyspeptic disorders of the upper gastrointestinal tract in a dose of 20 mg orally once daily. The effect of a single oral dose of esomeprazole 20 mg on preoperative gastric fluid pH and volume has not yet been studied. The second aim of this study was to determine whether or not a single oral dose of esomeprazole 20 mg, administered a night before surgery, is effective in increasing the pH $\geq 2.5$ and decreasing volume $\leq 0.4$ ml/kg or 25 ml in adult patients undergoing elective surgery by excluding those cases contaminated with duodenogastric reflux, if duodenogastric reflux significantly affects pH and volume of gastric contents.

Patients and methods

The protocol of the study was approved by the Research and Ethics Committee and written, informed patient consent was obtained. One hundred and twenty patients (120) of American Society of Anaesthesiologists (ASA) physical status I-II, aged 15–70 years scheduled for elective surgery under general anaesthesia participated in the study.

We excluded patients from our study known to have upper gastrointestinal disorders, the morbidly obese having a body mass index (BMI) of more than 40 kg/m², those receiving medications known to affect the secretory and/or motor functions of the stomach, difficult intubation, i.e. Mallampati class IV and/or mouth opening less than 5 centimetres and/or a thyromental distance less than 6.5 centimetres and/or history of documented difficult intubation, intestinal obstruction, parturients and Diabetes.
Mellitus. Patients who took the study drugs but their gastric aspirates showed bile acids due to duodenogastric reflux were not included in the final statistical analysis while analysing pH and volume of gastric contents. We did not consider these samples as true gastric contents because in these samples alkaline duodenal fluid was mixed with acidic gastric contents.

The patients were randomly allocated by sealed envelope method to receive either esomeprazole 20 mg (n = 60) or placebo (n = 60) by oral route at 9.00 pm on the night before surgery. All patients also received oral diazepam 10 mg at the same time. On the pre-operative anaesthesia visit, the nature and purpose of the study was explained to all patients. According to the hospital policy, all patients were fasted from 12 midnight irrespective of the nature (solids or liquids) of the last meal taken. Age, sex, weight, height, BMI, ASA physical status, and the drug given were recorded for each patient. Before the start of anaesthesia, all patients were asked if they had been aware of any unusual feelings (side-effects) after taking the medications, the night before surgery.

General anaesthesia was induced with injected fentanyl, propofol, and maintained with sevoflurane and air in oxygen. The lungs were ventilated taking care to avoid inflation of the stomach. Tracheal intubation was facilitated by rocuronium. Another endotracheal tube sized 8.5 mm internal diameter lubricated with paraffin liquid internally was passed in the oesophagus in accordance with their percentage. If bile salts are present in the surface, bile salts are absent. On the other hand, if bile salts are present the sulphur sinks down, sooner or later, in this test finely powdered sulphur is sprinkled upon the surface of cool (170°C or below) liquid. If the sulphur remains floating on the surface, bile salts are absent. On the other hand, if bile salts are present the sulphur sinks down, sooner or later, in accordance with their percentage. If bile salts are present in the fluid from 1:5000 (0.02% or 200 μg/ml) to 1:10,000 (0.01% or 100 μg/ml) sulphur at once begins to sink and is all precipitated in two or three minutes; even in a dilution of 1:120,000 (0.0008% or 8.33 μg/ml) precipitation occurs. Using bile salts as a marker for bile, we applied the qualitative Hay’s Sulphur test for the presence of bile salts. This test depends on the principal that bile salts have the property of reducing the surface tension of fluids in which they are contained. In this test finely powdered sulphur is sprinkled upon the surface of cool (170°C or below) liquid. If the sulphur remains floating on the surface, bile salts are absent. On the other hand, if bile salts are present the sulphur sinks down, sooner or later, in accordance with their percentage. If bile salts are present in the fluid from 1:5000 (0.02% or 200 μg/ml) to 1:10,000 (0.01% or 100 μg/ml) sulphur at once begins to sink and is all precipitated in two or three minutes; even in a dilution of 1:120,000 (0.0008% or 8.33 μg/ml) precipitation occurs.

Time since premedication, time since Nil per Os (NPO), pH, volume of gastric contents and the result of the Hay’s Sulphur test were also recorded for each patient. On the basis of Hay’s Sulphur test, we further divided Group C into Subgroups C-1 and C-2 and Group E into Subgroups E-1 and E-2 to observe

Table 1: Physical characteristics of patients and timing of events. (Values are expressed either as mean ±SD or numbers (percentage))

| Physical characteristics of patients | Group C n = 60 | Group E n = 60 | p value |
|-------------------------------------|----------------|----------------|---------|
| Age (years)                         | 34.78 ± 13.44  | 34.08 ± 10.25  | 0.7490  |
| Sex                                 |                |                |         |
| Male                                | 30 (50%)       | 30 (50%)       | 1.0000  |
| Female                              | 30 (50%)       | 30 (50%)       |         |
| ASA physical status                 |                |                |         |
| Class – I                           | 49 (81.66%)    | 44 (73.33%)    | 0.3822  |
| Class – II                          | 11 (18.33%)    | 16 (26.66%)    |         |
| Weight (kilograms)                  | 73.68 ± 15.28  | 78.47 ± 13.92  | 0.0753  |
| Height (centimetres)                | 161.31 ± 7.84  | 163.14 ± 10.63 | 0.2871  |
| Body Mass Index (kilograms/meter²)  | 28.40 ± 5.80   | 29.58 ± 5.43   | 0.2524  |
| Timings of events                   |                |                |         |
| Time since premedication (minutes)  | 832.25 ± 136.51| 812.50 ± 152.68| 0.4252  |
| Time since NPO (minutes)            | 661.85 ± 138.03| 656.33 ± 131.27| 0.3016  |
Table II: pH and volume of gastric contents. (Values are expressed as mean ± SD)

| Variables       | Group C                                    | Group E                                    |
|-----------------|--------------------------------------------|--------------------------------------------|
|                 | n = 60                                     | n = 60                                     |
|                 | Group C-1 n = 59                           | Group C-2 n = 39                           |
|                 | Group E-1 n = 58                           | Group E-2 n = 39                           |
| pH              | 3.06 ± 1.91                                | 1.90 ± 0.47                                |
| Volume (millilitres) | 38.72 ± 33.52                           | 19.60 ± 18.56                             |

Note: Samples mixed with blood (1 in Subgroup C-1 and 2 in Subgroup E-1) are not included. Group C-1 and Group E-1 represent contaminated samples with duodenogastric refluxate. Group C-2 and Group E-2 represent non-contaminated samples.

Comparison between Subgroups

Comparison of pH and volume between Group C-1 and Group C-2 (p value 0.0003 and 0.0016).
Comparison of pH and volume between Group E-1 and Group E-2 (p value 0.0041 and < 0.0001).
Comparison of pH and volume between Group C-2 and Group E-2 (p value < 0.0001 and 0.0068).

Table III: Patients at risk according to defined criteria. (Values are expressed as numbers (percentage))

| Variables               | Group C-2 n = 39 | Group E-2 n = 39 | p value |
|-------------------------|------------------|------------------|---------|
| Patients with pH ≤ 2.5  | 37 (94.87 %)     | 11 (28.20 %)     | <0.0001 |
| Patients with volume ≥ 25 ml | 12 (30.76 %)   | 1 (2.56 %)       | 0.0015  |
| Patients with pH ≤ 2.5 and volume ≥ 25 ml | 12 (30.76 %) | 1 (2.56 %)       | 0.0015  |

Note: Samples mixed either with duodenal contents (39) or blood (3) are not included.

Results

One hundred and twenty (120) adult inpatients undergoing elective neuro (n = 1), thoracic (n = 8), urology (n = 11), gynaecological (n = 14), orthopaedic (n = 28) and general (n = 58) surgery were enrolled. Physical characteristics of patients and timings of events are shown in Table I. There was no statistically significant difference between Groups C and E regarding age, weight, height, BMI, duration since premedication and duration since NPO.

We obtained gastric contents of all 120 patients. Three samples (2 in Group C and 1 in Group E) were mixed with blood. Hay’s test was performed on 117 samples and was positive in 39 (33%) patients (20 in Group C – 9 males and 10 females and 19 in Group E – 9 males and 10 females). These samples do not represent true gastric contents and, therefore, were considered as contaminated and are not included in final statistical analysis while analysing pH and volume of gastric contents.

Duodenogastric refluxate significantly affected the pH and volume of gastric contents in Subgroups C-1 and C-2 (p value 0.0003 and 0.0016) and in Subgroups E-1 and E-2 (p value 0.0401 and < 0.0001) as shown in Table II. The pH and volume of all the Subgroups C-1, C-2, E-1 and E-2 are also shown in Table II. There was a statistically significant difference between the Subgroups C-2 and E-2 (non-contaminated samples with duodenogastric refluxate) regarding pH (p 0.0118) and volume (p 0.0009) of gastric contents.

The proportion (percentage) of the patients considered “at risk” of significant lung injury should aspiration occur is shown in Table III after excluding samples contaminated with duodenogastric refluxate.

There was a statistically significant difference between the Subgroups C-2 and E-2 (p 0.0015) when both pH and volume were combined according to the criteria defined.

All patients were discharged from the hospital without any problem.

Discussion

Esomeprazole is the last of the five proton pump inhibitors (omeprazole, lansoprazole, pantoprazole and rabeprazole)
administered dose of proton pump inhibitors (omeprazole, esomeprazole, rabeprazole...etc and/or H₂-receptor antagonists (ranitidine HCl, nizatidine, famotidine...etc) a night before surgery on the intragastric pH and volume in adult patients undergoing elective surgery. A triple blind placebo controlled clinical trial. This project was approved by the College of Medicine Research and Ethics Committee King Saud University, Riyadh, Saudi Arabia. We studied five (5) proton pump inhibitors (omeprazole, lansoprazole, pantoprazole, rabeprazole and esomeprazole) and four (4) H₂ - receptors antagonists (ranitidine, famotidine, nizatidine and cimetidine) with one design, aim and research methodology.

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