A comparison of intravenous ranitidine and omeprazole on gastric volume and pH in women undergoing emergency Caesarean section

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We have compared the effect of intravenously administered omeprazole and ranitidine on gastric contents in a double-blind study in 80 consecutive women undergoing emergency Caesarean section. When the decision to perform emergency Caesarean section was made, patients were randomly assigned to receive either ranitidine 50 mg or omeprazole 40 mg intravenously. The volume and pH of the gastric contents were measured immediately after tracheal intubation and again before extubation. The gastric pH was found to be higher after omeprazole than after ranitidine immediately after intubation (5.89 ± 1.46 and 5.21 ± 1.36 respectively) ($P < 0.05$) and before extubation (5.97 ± 1.38 and 5.32 ± 1.24 respectively) ($P < 0.05$). However, the gastric volumes were comparable in both the groups. The number of patients with gastric volume >25 ml and pH <2.5 were 3 (7.5%) in the ranitidine group and 1 (2.5%) in the omeprazole group after intubation and none in either of the groups before extubation. We conclude that omeprazole 40 mg iv administered at the time of the decision to operate, results in higher gastric pH than ranitidine in obstetric patients undergoing emergency Caesarean section.

Une étude à double insu nous a permis de comparer l'effet de l'oméprazole et de la ranitidine sur le contenu gastrique de 80 parturientes subissant une césarienne d'urgence. Au moment de la prise de décision en faveur de la césarienne, les patientes ont été réparties aléatoirement pour recevoir soit de la ranitidine 50 mg, soit de l'oméprazole 40 mg par la voie intraveineuse. Le volume et le pH du contenu gastrique ont été mesurés immédiatement après l'intubation et avant l'extubation. Le pH gastrique était plus élevé après l'oméprazole qu'après la ranitidine immédiatement après l'intubation (respectivement 5.89 ± 1.46 et 5.21 ± 1.36 , $P < 0.05$) et avant l'extubation (respectivement 5.97 ± 1.38 et 5.32 ± 1.24 , $P < 0.05$). Cependant, le volume gastrique était comparable entre les deux groupes. Après l'intubation, le nombre de patientes avec un volume gastrique >25 ml et un pH <2.5 était de trois (7,5%) dans le groupe ranitidine, et de une (2,5%) dans le groupe oméprazole et d'aucune des deux groupes avant l'extubation. Les auteurs concluent que l'oméprazole 40 mg iv administré au moment de la décision d'opérer procurait un pH gastrique plus élevé que la ranitidine chez des parturientes subissant une césarienne en urgence.

Key words

ANAESTHESIA: obstetrics;

GASTROINTESTINAL TRACT: gastric volume, gastric pH;

PHARMACOLOGY: omeprazole, ranitidine.

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Accepted for publication 19th May, 1995.

Acid aspiration syndrome is an ever-present risk of general anaesthesia particularly in emergency and obstetrical situations, and the morbidity and mortality associated with this complication increases with the volume and acidity of the gastric aspirate.¹ A gastric pH <2.5 and volume >25 ml are suggested as being risk factors for the acid aspiration syndrome in humans.² One of the aims of preoperative treatment is to reduce these risk factors. Various regimens, which include antacids, anticholinergic drugs, H_2 receptor antagonists and the proton pump inhibitor, omeprazole, have been used to achieve this objective. However, at present, there is no unanimity on the optimum pharmacological regimen for patients

who require general anaesthesia for emergency Caesarean section.

The present study was designed to compare the effects of *iv* ranitidine and omeprazole on gastric volume and pH in patients undergoing emergency Caesarean section.

Methods

The study protocol was approved by the Hospital Ethics Committee and informed consent was obtained from all patients. Eighty consecutive healthy women with an uncomplicated singleton pregnancy who were at term and required emergency Caesarean section under general anaesthesia were selected for the study. Patients with a history of any acid-related gastrointestinal disease, recent gastric antisecretory drug therapy or any other medication which would interfere with gastrointestinal function were not included in the study. When the decision to perform Caesarean section was made, patients were randomly assigned to one of the two groups to receive a slow intravenous injection, over one minute, of either 50 mg ranitidine or 40 mg omeprazole in a double-blind manner.

Following preoxygenation for three minutes, anaesthesia was induced with thiopentone 4–5 mg · kg⁻¹ and succinylcholine 1.5 mg · kg⁻¹ was given to facilitate tracheal intubation. Cricoid pressure was applied at loss of the eyelash reflex and was maintained until the trachea was intubated securely. Further neuromuscular blockade was achieved with vecuronium 0.1 mg · kg⁻¹. Anaesthesia was maintained with 50% N₂O in O₂ and 0.5% halothane until delivery, after which N₂O was increased to 66%. At delivery, oxytocin 10 units and meperidine 0.5 mg · kg⁻¹ were given *iv*. At the end of surgery, atropine 0.02 mg · kg⁻¹ and neostigmine 0.05 mg · kg⁻¹ were given to reverse the residual neuromuscular blockade.

Gastric aspiration was performed immediately after tracheal intubation and again before tracheal extubation using a 16 FG double-lumen orogastric tube whose correct position in the stomach was confirmed by auscultation of injected air over epigastrium. The investigator taking the sample was unaware of the group to which the patient had been assigned. To obtain maximum yield, repeat aspiration was done after the tube was rotated and withdrawn 10 cm and readvanced. The volume of aspirate was recorded and pH measured with a Corning 150 pH meter. Patients whose gastric aspirate had a pH <2.5 and volume >25 ml were considered at risk of developing the acid aspiration syndrome according to criteria of Roberts and Shirley.²

Comparisons between groups were made using Student's *t* test for age, weight, fasting period and time intervals from injection of study drug to first gastric aspiration and first to second gastric aspiration. Analysis of variance was used for comparison of gastric pH and

TABLE I Patient data (mean ± SD)

	Ranitidine group (n = 40)	Omeprazole group (n = 40)
Age (yr)	27.50 ± 4.03	28.77 ± 4.38
Weight (kg)	53.07 ± 6.22	52.50 ± 5.20
Fasting period (hr)	12.00 ± 1.92	11.52 ± 2.07
Treatment to first gastric aspiration time (min)	67.12 ± 15.35	70.15 ± 16.69
First to second gastric aspiration time (min)	36.30 ± 5.10	34.50 ± 5.60

volume and Chi-square test with Yates' correction for incidence of patients at risk of acid aspiration syndrome. The values were considered to be statistically significant at *P* < 0.05.

Results

The two groups were comparable with respect to age, weight, fasting period and the time from injection of the study drug to first aspiration and first to second aspiration (Table I). The time from administration of the study drug to the first aspiration was not less than 35 min in any patient.

Gastric volumes were comparable between the groups immediately after tracheal intubation as well as before extubation. Post-intubation and pre-extubation mean pH values were higher in the omeprazole group than in the ranitidine group (*P* < 0.05) (Table II). Based on post-intubation aspirate, three patients (7.5%) were found to be at risk of aspiration syndrome in the ranitidine group and one patient (2.5%) in the omeprazole group. No patient in either of the groups was at risk before extubation. There was no difference between groups in the incidence of patients at risk of aspiration syndrome (volume >25 ml and pH <2.5) at any time. Among the patients considered to be at risk, the maximum time interval between administration of study drug to first aspiration was 45 min after ranitidine and 40 min after omeprazole.

As the aspiration after intubation might have influenced the aspiration values before extubation, the two were combined to produce a mean value for pH (calculated using H⁺ ion concentration) and total volume. Thus, had the volume of the first aspiration remained in the stomach, the number of patients at risk before extubation would have been two in the ranitidine group and one in the omeprazole group (NS). There were no cases of aspiration of gastric contents or any adverse effects.

Discussion

Pulmonary aspiration of gastric contents during anaesthesia is a small but important cause of anaesthesia-

TABLE II Gastric volume and pH (mean $\pm$ SD)

Group	Post-intubation		Pre-extubation	
	Volume (ml)	pH	Volume (ml)	pH
Ranitidine (n = 40)	17.02 $\pm$ 7.78	5.21 $\pm$ 1.36	6.02 $\pm$ 3.37	5.32 $\pm$ 1.24
Omeprazole (n = 40)	14.67 $\pm$ 6.50	5.89 $\pm$ 1.46*	7.10 $\pm$ 2.96	5.97 $\pm$ 1.38*

* $P < 0.05$.

related deaths, especially in obstetrics.³ Although precise numbers are not known, it is probable that many patients suffer nonfatal aspiration with considerable morbidity. Any safe treatment that reduces this hazard is desirable.

Efforts at preventing acid aspiration syndrome initially focused on increasing gastric pH > 2.5 with oral antacids given before general anaesthesia in obstetric situations. However, antacids are reported to increase gastric volume.^{4,5} Various clinical reports described severe pulmonary disturbances^{6,7} and even death⁸ following aspiration of gastric contents containing antacids. Administration of H_2 -receptor antagonists increases gastric pH and decreases gastric volume.⁹⁻¹¹ Nevertheless, some patients have been reported to have gastric pH < 2.5 even after the use of an H_2 -receptor antagonist.

Omeprazole, a substituted benzimidazole derivative, is a new gastric antisecretory agent which decreases gastric secretion by inhibiting the activity of H^+/K^+ ATPase, the proton pump of the parietal cells. It is more potent than H_2 -receptor antagonist because it acts on the final step in the stimulatory process for acid secretion.¹²

Omeprazole as a gastric antisecretory agent has been clinically evaluated in obstetric as well as non-obstetric situations but previous reports of oral omeprazole have had conflicting results. Moore *et al.*¹³ reported that omeprazole, 80 mg *po* the night before elective Caesarean section, failed to produce gastric volume < 25 ml and pH > 2.5 in seven of 20 patients at induction of anaesthesia. Conversely, Gin *et al.*¹⁴ did not find any patient with a low gastric pH and high volume when omeprazole was given orally twice before elective Caesarean section. Recently, Orr *et al.*¹ reported that 87% of patients who received omeprazole, 40 mg *po* at bedtime and again in the morning before elective Caesarean section, had gastric contents in a safe range.

We preferred to administer ranitidine and omeprazole *iv* because this offers the advantage of improved bioavailability in emergency obstetrical situations, where delayed gastric emptying might render oral medication less effective when it is most required. Further, omeprazole is rapidly inactivated in the acidic gastric environment¹⁵ and its enteric coating may cause delay in absorption.¹⁶

Using *iv* omeprazole, 40 mg at the time of decision to operate, Rocke *et al.*¹⁷ found a reduction in the risk of acid aspiration. Using at-risk criteria of pH < 3.5 and volume > 25 ml, they found four (1.42%) patients after intubation and two (0.7%) patients before extubation at risk of acid aspiration. However, only one patient (0.35%) after intubation and none before extubation was at risk when the at-risk criteria of pH < 2.5 and volume > 25 ml was used. They further found that had the first aspiration remained in the stomach, three (1.06%) patients would have been at risk (pH < 2.5 and volume > 25 ml) at the time of extubation. Our observations in the omeprazole group are consistent with those of Rocke *et al.*¹⁷ However, in addition, their patients were given metoclopramide 10 mg *iv* five minutes after omeprazole administration and 30 ml 0.3 M sodium citrate on entry to the operating room. We speculate that addition of metoclopramide and sodium citrate to the omeprazole regimen has no advantage.

Although most studies have shown omeprazole to be a good prophylactic regimen against acid aspiration syndrome, Yau *et al.*¹⁸ observed a higher incidence of patients at risk of aspiration who received omeprazole than ranitidine when administered orally in patients undergoing emergency Caesarean section. This may have been because omeprazole is rapidly inactivated in acidic gastric environment¹⁵ and variable absorption resulting from delayed gastric emptying during labour.

The technique we used to measure the volume of gastric contents may underestimate the actual volume but it is a valid and accepted method¹⁹ and commonly used in similar studies. Also, the sampling error, if any, should be small and consistent between the two groups.

In conclusion, intravenous omeprazole given at the time of decision to perform emergency Caesarean section, produced a higher gastric pH at induction of anaesthesia than *did* intravenous ranitidine and this difference was maintained up-to the time of extubation. However, there was no difference in gastric volume and the number of patients deemed to be at risk for acid aspiration syndrome. The improvement in pH by omeprazole though significant statistically, is clinically not significant and in

view of its high cost, the authors feel that omeprazole is not a cost-effective drug. We suggest further studies to determine the effect of adding oral antacids and metoclopramide to omeprazole administered intravenously as part of the treatment to prevent acid aspiration syndrome in patients undergoing emergency Caesarean section.

Acknowledgments

The authors wish to thank Mrs. Abha Agarwal, Research Officer, Institute for Research in Medical Statistics, New Delhi, for her expert advice in statistical analysis.

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