Gastric fluid volume, pH, and emptying in elective inpatients. Influences of narcotic-atropine premedication, oral fluid, and ranitidine

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One hundred and twenty healthy, elective surgical inpatients were randomly assigned to one of four groups. Between two and three hours before the scheduled time of surgery all patients ingested a marker dye, phenol red, 50 mg in 10 ml water, with placebo tablet alone (Groups 1 and 2), placebo tablet with 150 ml oral fluid (Group 3), or oral ranitidine 150 mg with oral fluid 150 ml (Group 4). Patients in Group 1 received oral diazepam or no premedication, while those in Groups 2, 3, and 4 received IM narcotic and atropine one hour preoperatively. Following induction of anaesthesia the residual gastric fluid was aspirated through a Salem sump tube and its volume, pH, and phenol red content measured. Mean volumes were Group 1: 24 ml; Group 2: 13 ml; Group 3: 17 ml; Group 4: 14 ml. Mean pH values were Group 1: 2.99; Group 2: 3.03; Group 3: 3.44; Group 4: 5.28. The amount of phenol red in the samples indicated at least 90 per cent gastric emptying had occurred in 90 per cent of patients. We conclude that, in healthy patients, 150 ml oral fluid is almost completely emptied from the stomach within two hours of ingestion, even when followed one hour later by narcotic-atropine premedication.

Key words

ANAESTHESIA: inpatient, general, adverse effects;
GASTROINTESTINAL TRACT: gastric pH, gastric volume, gastric emptying; PNEUMONIA: aspiration, prevention and control; NARCOTICS: adverse effects; RANITIDINE: therapeutic use.

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Experimental work in animals, when extrapolated to humans, suggests that severe pulmonary acid aspiration syndrome will result if a patient aspirates $0.4 \text{ ml} \cdot \text{kg}^{-1}$ of gastric fluid with pH less than 2.5.¹ These values are commonly quoted by investigators who describe prophylactic regimes which might reduce the incidence of this dreaded complication of anaesthesia. Clinical studies have demonstrated that overnight fasting does not ensure an empty stomach at the time of surgery.²⁻⁴ Nevertheless, acid aspiration syndrome is rare in healthy, elective patients⁵ and, although one third of patients may be "at risk," investigators have invariably used control groups in this category.

Ingestion of oral fluid between two and four hours before induction of anaesthesia has no significant effect on either mean residual gastric fluid volume (RGV) or pH at the time of surgery.⁶⁻⁹ Prolonged fasting is therefore of no benefit to healthy elective patients, whereas oral ranitidine has been shown to reduce both volume and pH of gastric contents, even with preoperative fluid ingestion.⁷⁻¹⁰

Recently Manchikanti *et al.* have shown that narcotic premedication does not increase RGV, even though this group of drugs is known to delay gastric emptying.¹¹ All their patients had fasted for at least eight hours. To determine if this were also true following preoperative ingestion of fluids, we investigated the effect of narcotic-atropine premedication on the volume and pH of gastric fluid at the time of surgery in patients given oral fluid with or without ranitidine 2-3 hr preoperatively. Gastric emptying of the ingested fluid was assessed using phenol red as a marker dye.

Methods

The study protocol was approved by the University of Calgary Conjoint Ethics Committee. Informed consent was obtained from 122 inpatients, age 18-70 yr, ASA physical status I or II, who were scheduled for elective

TABLE I Randomised groups

	<i>n</i>	Fluid (ml)	Tablet	Premedication
Group 1	29	0	Placebo	Diazepam or nil
Group 2	28	0	Placebo	IM narcotic-atropine
Group 3	29	150	Placebo	IM narcotic-atropine
Group 4	31	150	Ranitidine	IM narcotic-atropine

surgical procedures at 10:00 h or later. Pregnant and emergency patients were excluded, as were those taking medication known to affect gastric secretion or motility. Patients' age, sex, weight, duration of overnight fast, smoking habit and history of heartburn were recorded. They were then randomized to one of four groups (Table I) using a table of random numbers. Between two and three hours before the scheduled time of surgery all patients ingested 10 ml water containing 50 mg phenol red (phenolsulphonphthalein, Sigma Chemicals P4758), a marker dye used to measure gastric fluid volume.¹²⁻¹⁴ This was taken with a placebo tablet alone (Groups 1 and 2), placebo tablet with oral fluid 150 ml (Group 3), or ranitidine 150 mg PO with 150 ml oral fluid 150 ml (Group 4). Ingestion was observed by one of the investigators. Patients were allowed to choose water, fruit juice, coffee or tea. Patients in Groups 2, 3, and 4 received IM morphine 7.5–15 mg with atropine 0.4–0.6 mg approximately 1 hr before surgery. Six patients who were intolerant of morphine received meperidine 50–100 mg. Those in Group 1 received either oral diazepam 7.5–15 mg 90 min preoperatively, or no premedication.

Following induction of anaesthesia, a #18 FG Salem-sump tube was passed into the stomach and its position confirmed by auscultation for insufflated air. Gastric fluid was aspirated into a 60 ml syringe with the patient in the supine position and with the sampling tube in several locations within the stomach. The investigator taking the sample was unaware of the group to which the patient had been assigned. Residual gastric fluid volume (RGV) was recorded, and its pH was measured using a calibrated Corning 150 pH meter. The phenol red concentration was measured in alkalized solution using a Beckman DU-50 spectrophotometer at 560, 520, and 600 nm.¹⁴ The lower limit of detection was $5 \mu\text{g}\cdot\text{ml}^{-1}$. The concentration of dye was multiplied by the volume of aspirate; from this

the percentage of ingested dye, and therefore fluid, which was in the stomach was calculated. This figure gave an estimate of the degree of gastric emptying.

Results from 117 patients were analyzed; those from five patients in whom the interval from ingestion of dye to sampling exceeded four hours were excluded. Demographic data are given as means and standard deviation. Values for RGV and pH are given as means and ranges. Tests of significance among groups were performed using one-way analysis of variance for parametric data, and the Mann-Whitney U test for non-parametric data. Differences were considered statistically significant when $p < 0.05$.

Results

The four groups were comparable with respect to age, weight, and duration of overnight fast from the last intake of fluid until ingestion of phenol red, tablet, and oral fluid (Table II). The time from ingestion to narcotic-atropine premedication in Groups 2–4 was similar. Although the time of ingestion was 2–3 hr before the scheduled time of surgery, the actual ingestion-sampling interval ranged from 1.3 through 4.0 hr. Mean fast for patients who received only marker dye and tablet (Groups 1 and 2) was approximately 14 hr, compared with approximately 2.5 hr for those who drank 150 ml fluid (Groups 3 and 4).

Mean RGV was highest in patients in Group 1 who fasted and did not receive narcotic or atropine (Table III). It was significantly lower in patients in Groups 2, 3, and 4 who received narcotic-atropine premedication ($p < 0.001$). Mean pH value in patients who received ranitidine (Group 4) was significantly higher than in the other three groups (Table IV) ($p < 0.001$). There was a wide range of values of both volume and pH in all four groups, but only ten per cent of patients who received ranitidine had a gastric fluid pH < 2.5 . In patients who ingested fluid (Groups 3 and 4) neither volume nor pH of gastric fluid correlated with the type of ingested fluid. There was no significant difference in RGV or pH between patients with heartburn and those without, nor between smokers and nonsmokers. Table IV records the number of patients in each group whose gastric aspirate contained one, one to five, and five per cent of ingested phenol red. In 34 of the 60 samples in Groups 3 and 4 no dye was detected. More than

TABLE II Patient characteristics (mean $\pm$ SD)

	Age (yr)	Weight (kg)	Overnight fast (hr)	Ingestion – narcotic (hr)	Ingestion – sample (hr)	Total fast (hr)
Group 1	41 $\pm$ 13	71 $\pm$ 12	12.3 $\pm$ 1.7	—	2.4 $\pm$ 0.6	14.6 $\pm$ 1.7
Group 2	41 $\pm$ 12	67 $\pm$ 15	11.3 $\pm$ 1.4	1.2 $\pm$ 0.4	2.6 $\pm$ 0.7	13.9 $\pm$ 1.5
Group 3	45 $\pm$ 16	73 $\pm$ 16	11.8 $\pm$ 1.8	1.2 $\pm$ 0.4	2.7 $\pm$ 0.8	2.7 $\pm$ 0.8
Group 4	44 $\pm$ 17	73 $\pm$ 16	12.2 $\pm$ 3.1	1.2 $\pm$ 0.5	2.6 $\pm$ 0.6	2.6 $\pm$ 0.6

TABLE III Gastric fluid volume

	Volume (ml) mean (range)	% patients vol > 25 ml
Group 1 (fast)	24 (0-90)*	50
Group 2 (fast)	13 (0-70)	16
Group 3 (fluid)	17 (0-131)	21
Group 4 (fluid)	14 (0-51)	23

$p < 0.001$ Group 1 vs Groups 2, 3, and 4 (Mann-Whitney U test).

five per cent retrieval, representing approximately 7.5 ml of 150 ml ingested fluid was obtained in only four of the 60 patients.

Discussion

Several studies have demonstrated the futility of prolonged fasting in an attempt to ensure an empty stomach. Metoclopramide, by increasing the rate of gastric emptying, reduces the volume of gastric fluid.¹⁵ Oral antacids such as sodium citrate neutralize gastric acid but they do not reduce the volume.¹⁶ Furthermore, their effect is short lived and they do not inhibit secretion of pepsin which may play a major part in the severity of the acid aspiration syndrome.¹⁷ The H_2 receptor antagonist, ranitidine reduces secretion of gastric acid and pepsin,¹⁷ and its effect lasts for several hours.¹⁸ Experiments in animals suggest that pulmonary aspiration of even very small volumes of fluid with a pH value < 1.5 is more dangerous than aspiration of much larger volumes of fluid with a pH value > 3.0.¹⁹

Previous studies from our centre⁷⁻¹⁰ were conducted on patients who received either oral diazepam or no premedication. Those findings were not extrapolated to patients who receive narcotic-atropine premedication because both these drugs delay gastric emptying.²⁰ However, if there is an interval of one hour between

Table V Phenol red retrieval

	Phenol red		
	>5%	1-5%	<1%
Group 1	4	2	23
Group 2	4	7	17
Group 3	2	7	20
Group 4	2	5	24

Numbers in columns represent number of patients in each range.

ingestion of fluid and narcotic-atropine premedication, gastric emptying should be nearly complete before those drugs produce their effects. This was confirmed by the finding that only four of 60 patients in Groups 3 and 4 had more than five per cent of ingested phenol red in the gastric aspirate. A small amount of phenol red is absorbed from the stomach, but approximately 90 per cent is retrieved from watertight Heidenhain gastric pouches in dogs,²¹ thus making it a satisfactory marker dye for estimation of gastric emptying. In our study, RGV comprised mainly gastric secretions. In more than 50 per cent of the patients in Groups 3 and 4 no phenol red was detected, and therefore none of the ingested fluid remained in the stomach. Indirect evidence of rapid gastric emptying is provided by the effectiveness of oral ranitidine in raising gastric pH, because the drug must pass into the small bowel to be absorbed before it can exert its pharmacological effect.²² Both morphine and atropine reduce gastric acid secretion in addition to slowing gastric emptying.²³ Thus lower mean RGV, but greater dye retrieval in some patients, was found in Group 3 than in comparable patients in a previous study who did not receive narcotic-atropine premedication.^{7,8} The slightly greater retention of ingested fluid was apparently more than offset by diminished gastric secretion. The reduction in secretion would explain why mean RGV was lower in Group 2 than in Group 3. In each study we aspirated gastric contents through a multi-orifice Salem-sump tube, which gives a small but fairly consistent underestimate of the true RGV, and is as accurate as a dye dilution method.²⁴

The differences in pH values were statistically significant between the ranitidine group only (Group 4) and the other three groups. Nevertheless, the number of patients "at risk" with RGV > 25 ml and pH < 2.5 was highest among those who followed the fasting guidelines of "NPO after midnight" and received oral diazepam, or no premedication.

The Canadian Anaesthetists' Society guidelines recommend a minimum of five hours for preoperative fasting,²⁵ with the warning that complete emptying of the stomach cannot be guaranteed in the presence of pain, trauma,

TABLE IV pH values and "high risk" factors

	n*	pH		Percentage of patients	
		mean	(range)	pH < 2.5	High risk†
Group 1 (P)	28/29	3.05	(2.22-7.71)	66	33
Group 2 (P)	24/28	2.89	(1.53-7.80)	39	16
Group 3 (P)	23/29	3.44	(1.68-7.32)	33	17
Group 4 (R)	25/31	5.28	(1.52-7.41)‡	10	10

P = placebo; R = ranitidine.

*The difference between numerators and denominators represents patients in whom no gastric fluid could be obtained.

†Gastric fluid volume 25 ml and pH 2.5.

‡ $p < 0.001$ Group 4 vs Groups 1, 2, and 3 (Mann-Whitney U test).

apprehension, narcotics, gastrointestinal disorders, pregnancy, or medications. We submit that complete emptying of the stomach can never be guaranteed. The elective patient who fasts for 12 hr is at no less risk from pulmonary acid aspiration syndrome than the one who drinks fluid until two hours before surgery. However, because RGV is so variable, it is difficult to predict either safety or high risk in the individual patient.

We conclude that gastric fluid volume and acidity at induction of anaesthesia are not significantly altered by the ingestion of 150 ml water, coffee, tea or fruit juice 2–3 hr preoperatively, nor by a narcotic-atropine premedication. We have not investigated the effects of other fluids, especially those which contain substantial quantities of fat such as milk. Healthy, elective patients should be permitted to take oral fluid until 2–3 hr before their scheduled time of surgery. Because of the very low incidence of the pulmonary acid aspiration syndrome in this category of patients, we recommend routine H₂ receptor antagonist treatment only for patients who are pregnant, morbidly obese or who have other pathology which might place them in the high-risk category for regurgitation and aspiration of gastric contents.

Acknowledgments

The authors thank Glaxo Canada Ltd. for supplying ranitidine and matching lactose-filled placebo tablets; anaesthetists, surgeons, and nursing staff for their cooperation; Mr R. D. Kirk, gastrointestinal unit faculty technician, for laboratory analyses; and Miss J. Lekopoy for secretarial assistance.

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Résumé

Cent vingt patients en bonne santé devant subir une chirurgie élektive ont été, après randomisation, divisés en quatre groupes. Entre deux et trois heures avant la chirurgie tous les patients ont ingéré un marqueur, du phénol rouge, 50 mg dans 10 ml d'eau avec du placebo seul (Groupe 1 et 2), placebo et 150 ml de liquide (Groupe 3), ou de la ranitidine par voie orale 150 mg avec 150 ml de liquide (Groupe 4). Les patients du Groupe 1 ont reçu du diazépam par voie orale ou n'ont pas reçu de prémédication, alors que les patients du groupe 2, 3 et 4 ont reçu une injection intramusculaire de narcotiques additiomée d'atropine une heure avant l'opération. Après l'induction de l'anesthésie le liquide gastrique résiduel était aspiré et son volume, pH, et le contenu du phénol rouge mesuré. Les volumes moyens étaient pour le Groupe 1: 24 ml; Groupe 2: 13 ml; Groupe 3: 17 ml; Groupe 4: 14 ml. Les valeurs moyennes du pH étaient Groupe 1: 2.99; Groupe 2: 3.03; Groupe 3: 3.44; Groupe 4: 5.28. La quantité de phénol dans les échantillons indiquaient qu'au moins 90 pour cent de vidange gastrique est survenue chez 90 pour cent des patients. On conclut que chez des patients en bonne santé, 150 ml de liquide ingéré par voie orale est presque complètement absorbé en dedans de deux heures même après avoir administré une prémédication au narcotique-atropine.