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The influence of posture on the gastric emptying of antacids

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Summary

The gastric emptying of two radiolabelled antacid preparations has been monitored by gamma scintigraphy with subjects in 3 postures; supine, lying on their left sides and lying on their right sides. Aluminium hydroxide- and alginate-based formulations have been radiolabelled with indium-113m and administered to healthy volunteers following a liquid meal. The antacid containing aluminium hydroxide mixed and emptied with the other stomach contents. The raft-forming alginate formulation emptied faster than the food in subjects lying on their left sides, and slower in subjects lying on their right sides. Thus the protection afforded by alginate-based preparations in the treatment of oesophageal reflux may be strongly influenced by posture.

Introduction

The efficacy of an antacid preparation is influenced both by its acid binding capacity and the rate of gastric emptying. Following administration to fasted subjects antacids may empty relatively rapidly from the stomach (Jenkins et al., 1983) and hence have only a limited duration of action.

The composition of the preparations has a marked effect on the gastric residence. Alginate-based formulations tend to float on the other gastric contents and remain

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in the stomach until most of the food has emptied (May et al., 1984). This may be of therapeutic advantage in the treatment of reflux oesophagitis. It has been demonstrated that the alginate raft formed in the stomach refluxes preferentially, and thereby protects the oesophagus from the more acidic gastric contents (Mahmud et al., 1979). Alginate-based formulations have been reported not to neutralize appreciably the gastric acid (Williams et al., 1979). The duration of the protection afforded by the alginate preparations may be enhanced by the slower than average gastric emptying rates exhibited by patients with gastro-oesophageal reflux (Baldi et al., 1981; McCallum et al., 1981).

Most in vivo studies of antacids have been carried out with the subjects in an upright position (standing or seated). Patients taking antacids, however, may be bed-ridden or may take a dose immediately prior to retiring for the night. In a recumbent position there will be a slower drainage of refluxed stomach contents from the oesophagus and hence prolonged exposure of the oesophageal mucosa to acidic solutions (Johnson et al., 1978). Additionally, the influence of posture may prevent antacid rafts from protecting the oesophagus. Yu (1975) measured faster gastric emptying when infants were lying prone or on their right sides, than when supine or on their left sides. In babies, however, Blumenthal et al. (1979) found no appreciable differences in gastric emptying rates for these 4 positions. Vagotomy and pyloroplasty resulted in much more rapid gastric emptying in patients in the upright position compared with the rates measured with them lying on their left sides, although there had been little difference between the two rates pre-operatively (McKelvey et al., 1969). Similar findings have been reported by Hancock et al. (1974) when comparing patients in supine and upright postures.

The present study has been undertaken to compare the gastric emptying of antacid preparations in 3 recumbent postures. Two formulations have been investigated; one has been shown previously to mix with food in the stomach, and the other to form a raft (May et al., 1984).

Materials and Methods

Materials

The gastric emptying of two antacid formulations, Asilone Suspension (Berk Pharmaceuticals, Shalford) and Liquid Gaviscon Suspension (Reckitt and Colman Pharmaceutical Division, Hull) were investigated. The Asilone Suspension (Asilone) contained 840 mg dried aluminium hydroxide B.P., 270 mg activated dimethicone and 140 mg light magnesium oxide B.P. in 10 ml; and the Liquid Gaviscon Suspension (Gaviscon), 500 mg sodium alginate B.P.C. and 267 mg sodium bicarbonate Ph.Eur. in the same volume.

Indium-113m was used to radiolabel both preparations. The radionuclide was obtained by the elution of an indium-113m generator (Amersham International, Amersham) with 0.04 M hydrochloric acid. Asilone was radiolabelled by addition of co-precipitated indium and aluminium hydroxides, as described previously (Jenkins et al., 1983; May et al., 1984). Indium-113m labelled alginic acid was used to radiolabel the Gaviscon. To a solution of 15 MBq indium-113m chloride in 0.5 ml

0.04 M hydrochloric acid was added 250 mg alginic acid powder suspended in 2.5 ml distilled water. The mixture was stirred for 30 min, centrifuged, and the precipitate suspended in 5 ml water, followed by further centrifuging. This precipitate was suspended in 5 ml sodium bicarbonate solution at pH 8, centrifuged, then suspended in 5 ml hydrochloric acid at pH 2 and centrifuged again. The resulting [^{113m}In]labelled alginic acid was suspended in 3 ml water and made up to 10 ml with Gaviscon. Approximately 70% of the radioactivity was associated with the initial precipitate, and each subsequent washing leached about 10% of the radioactivity from the solid.

Clinifeed ISO (Clinifeed) (Rousell Laboratories, Wembley Park) provided a homogeneous 375 ml liquid meal with an energy content of 1575 kJ. The Clinifeed was radiolabelled by the addition of 1 ml [^{99m}Tc]labelled diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) solution (CIS (U.K.), London).

Methods

Nine healthy male volunteers aged 20–24 years participated in this study, after giving written informed consent. The gastric emptying of the radiolabelled preparations was monitored with volunteers lying in one of 3 positions: supine, on their right sides and on their left sides. A group of 5 subjects was studied in the same posture on two occasions; Asilone being taken during one experiment and Gaviscon during the other.

Each subject fasted for at least 4 h prior to each experiment. An anatomical reference marker radiolabelled with technetium-99m was taped to his skin anteriorly over the right lobe of his liver. With the subject lying in the test position he was instructed to drink 375 ml Clinifeed containing 3 MBq [^{99m}Tc]DTPA. Thirty minutes after taking the Clinifeed he drank a 10 ml dose of an antacid preparation radiolabelled with 3 MBq indium-113m. The subject remained in the same position throughout the period of the experiment.

Anterior images of the stomach were recorded for 60 s at approximately 10 min intervals, using a gamma camera having a 40 cm field of view and fitted with a medium energy (400 keV maximum energy) parallel hole collimator. The data were stored by computer for subsequent analysis. The indium-113m and technetium-99m distributions were imaged simultaneously and recorded separately by the computer. One week later the experiment was repeated, but with the subject taking the alternative antacid.

For each image the amount of radionuclide in the stomach was assessed by defining a region of interest around the stomach area in the image displayed by computer on a television monitor. The sizes and shapes of the stomachs were identified from the earlier images and related to the positions of the anatomical markers. The indium-113m count rates were corrected for background counts and for radioactive decay, and expressed as a percentage of the count rates from the stomach 15 min following antacid administration. The technetium-99m count rates were corrected for background counts, radioactive decay and also for counts arising from the presence of indium-113m. The gastric emptying of the Clinifeed was calculated for the same time periods as the antacid emptying, and also from the time of Clinifeed dosing.

Results

The rates of gastric emptying of the antacids have been compared with those of the Clinifeed meal. The results for the 3 postures are shown in Fig. 1. The values have been expressed as proportions of each preparation remaining in the stomach 15 min after taking the antacids. Thus it is possible to compare directly the relative residence times of the materials in the stomach.

In the supine posture both antacid preparations emptied from the stomach at approximately the same rate as the liquid meal. The Gaviscon, however, emptied more rapidly than either the Asilone or the Clinifeed when the subjects were lying on their left sides. With the volunteers lying on their right sides little Gaviscon emptying occurred until most of the Clinifeed had left the stomach. For all postures the Asilone emptied from the stomach at approximately the same rate as the Clinifeed. In general, there was little difference between the emptying rates of the liquid meal when measured in the presence of Asilone or Gaviscon.

The data in Table 1 show that on average about 75% of the Clinifeed remained in the stomach at the time of the antacid administration. The volumes of the stomach contents were similar on both occasions. Any differences in gastric emptying patterns between the 3 postures during the initial 30 min were masked by inter-subject variability. Subsequently the Clinifeed appeared to empty fastest in subjects lying on their right sides and slowest in those lying on their left sides.

TABLE 1

VOLUME OF CLINIFEED IN THE STOMACH AT THE TIME OF ANTACID ADMINISTRATION

Posture	Subject	Clinifeed volume (ml)	
		Antacid	
		Asilone	Gaviscon
Supine	1	285	245
	2	325	263
	3	337	285
	mean	316	264
Lying on left side	4	315	360
	5	315	262
	6	295	244
	mean	308	288
Lying on right side	7	300	240
	8	281	337
	9	247	270
	mean	276	282

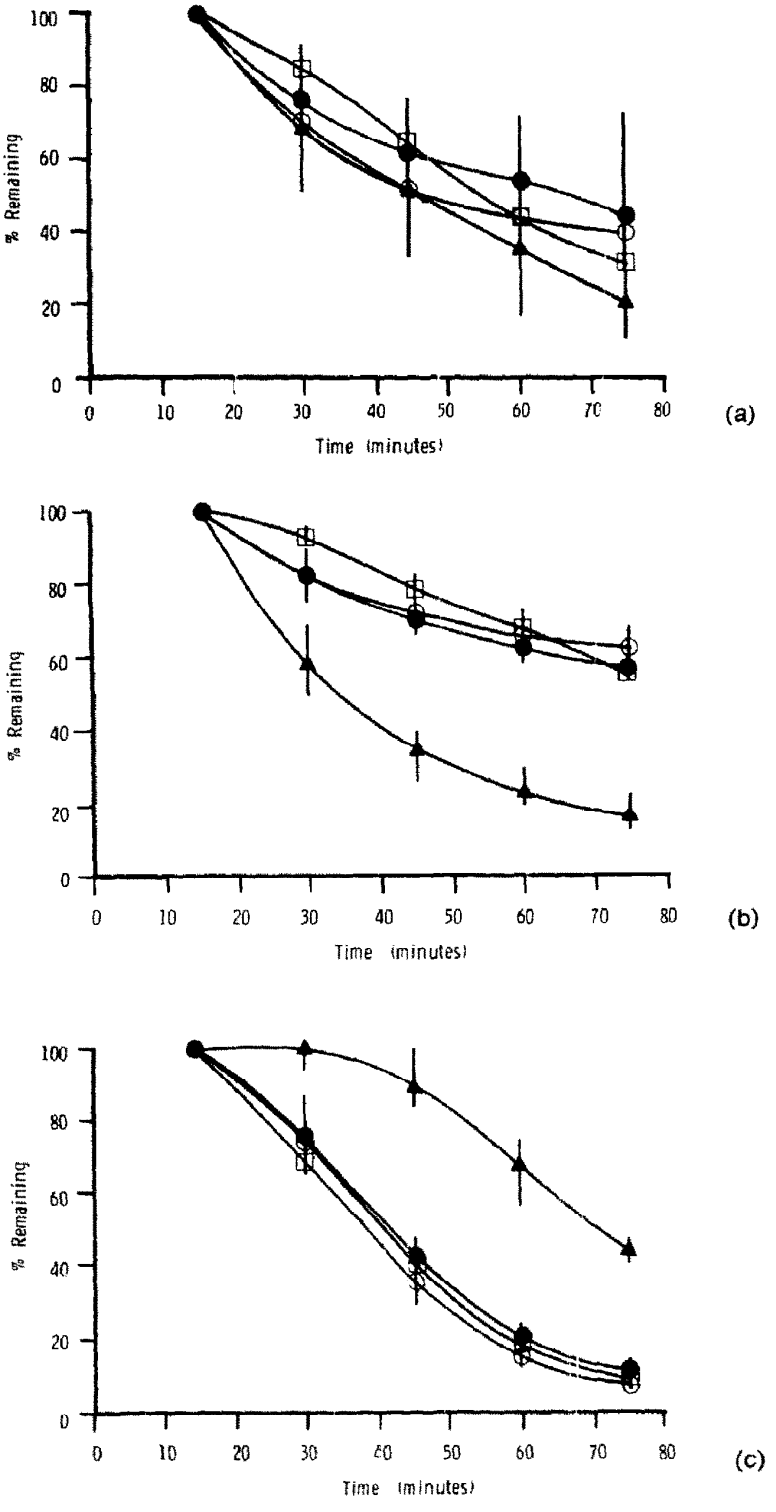

Fig. 1. Gastric emptying of Clinifeed, Asilone and Gaviscon administered to subjects lying (a) supine, (b) on their left sides and (c) on their right sides. The mean values are shown along with the ranges (n = 3 for each posture). Asilone, ○; Gaviscon, ▲; Clinifeed in the presence of Asilone, ●; and Gaviscon, □.

Discussion

Previous studies (Malmud et al., 1979; May et al., 1984) have shown that alginate-based formulations tend to float on the other stomach contents, and that Asilone mixes with the Clinifeed liquid meal. The results of the present investigation are consistent with these observations. With subjects lying on their right sides the floating alginate layer was towards the greater curvature of the stomach and thus away from the pylorus. Only when the volume of stomach contents was relatively low was the alginate able to pass into the duodenum. The opposite situation occurred in subjects lying on their left sides. Part of the alginate layer was between the food and the pylorus, and thus emptied preferentially. In the supine posture, all 3 preparations had similar access to the pyloric antrum and emptied at approximately equal rates. In all 3 postures the Asilone emptied at the same rates as the Clinifeed.

For the accurate measurement of gastric emptying rates, a combination of anterior and posterior imaging is required in order to correct for anterior and posterior movements of the tracers within the stomach (Tothill et al., 1980). In the present study, the need for the subjects to remain in the desired position throughout each experiment precluded bidirectional monitoring. Since the conditions were the same for each pair of experiments valid comparisons of the relative emptying rates of the two antacids could be achieved. Each subject was studied in only one posture in order to maintain the radiation doses well within acceptable limits. Based on the data of Siegel et al. (1983) it is estimated that each volunteer received a total radiation dose of 0.7 mGy to his stomach and 1.4 mGy to his small intestine.

For each posture the average gastric emptying rates of the Clinifeed were similar when taken with either antacid. Since studies in each posture were carried out with different groups of subjects, the differences between the Clinifeed emptying rates for the 3 positions were not statistically significant. Gastric emptying of the liquid meal, however, appeared to be fastest for subjects lying on their right sides. In the supine position the emptying rate was approximately the same as that measured by May et al. (1984) in subjects in an upright position.

The results of this study indicate that for recumbent patients the alginate rafts are unlikely to provide protection against reflux of the acidic stomach contents into the oesophagus. Preparations which exert little neutralizing action on the gastric acid are expected to be relatively ineffective in this situation. It is possible, however, that patient movement may disrupt the rafts releasing alkaline ingredients from the formulations to react with the acid. Williams et al. (1979) reported that Liquid Gaviscon provided relief from the common symptoms of gastro-oesophageal reflux both during the day and at night. The validity of these findings is questionable since there was no control group in the trial. The results of the present study indicate that preparations which neutralize the acidic gastric contents are likely to be the most efficacious in recumbent patients with reflux oesophagitis.

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