Gastric emptying of two radiolabelled antacids

J Monés, I Carrió, M Roca, M Estorch, R Calabuig, S Sainz, C Martinez-Duncker, F Vilardell

Abstract

The rate of gastric emptying of two antacids, magaldrate and Maalox, was investigated using scintigraphy. Successful labelling of the antacids was carried out with \(^{99}\)Tc. The stability of the \(^{99}\)Tc-labelled antacids was satisfactory and there was no difference in antacid capacity between the labelled and unlabelled antacids. The studies were carried out on 15 healthy male volunteers. After an eight hour fast each subject ingested a standardised meal of 95-7 MJ (400 kcal). One hour later 10 ml of one of the two antacids previously labelled with \(^{99}\)Tc was administered. Serial detection by anterior and posterior projection of the amount of antacid retained in the stomach was performed to determine gastric emptying of antacid. One week later the study was repeated under the same conditions with the other antacid also labelled with \(^{99}\)Tc. The mean (SD) percentages of antacid retained in the stomach fit a linear model with a t1/2 of 86-6 (15-3) minutes for magaldrate and 52-3 (5-2) minutes for Maalox (p<0.01). When the mean percentages of retention at six time intervals were compared for both antacids, it was found that Maalox emptied much faster (p<0.01 at 15 and 30 minutes, p<0.02 at 45, 60, 75, and 90 minutes).

The effectiveness of antacids in healing duodenal ulcer is well documented. Until a few years ago this was thought to be directly related to the complete neutralisation of gastric pH, which required high dosages (210 ml/day capable of neutralising 800-1000 mmol HCl/day). More recent studies have shown that lower dosages of antacids are also therapeutically effective, perhaps because these drugs seem to stimulate the protection and repair of the gastric mucosal membrane in experiments carried out in both animals and humans. It has been shown that the aluminium in antacids stimulates protection of the gastric mucosa through dependent as well as independent mechanisms of prostaglandin release.

The aim of the study was to assess the gastric emptying of two different antacids under physiological conditions using a scintigraphic technique.

ANTACIDS

Commercial doses of antacids (10 ml samples) were used. Magaldrate (Boehringer-Mannheim Laboratories) is a chemical combination of magnesium hydroxide and aluminium hydroxide. A comparison of the x rays of the magaldrate dosage form and hydroxinate clearly shows that magaldrate has a hydrotalcite-like structure, with sulphate as the major interlayer anion and carbonate present in the interlayer space. A 10 ml sample containing 800 mg magaldrate has a theoretical neutralisation capacity of 26-20 mEq/HCl. Maalox (Rorer Laboratories) is an aluminium hydroxide-magnesium hydroxide gel in suspension. A 10 ml sample contains 450 mg aluminium hydroxide and 400 mg magnesium hydroxide with a theoretical neutralisation capacity of 26-00 mEq/HCl.

LABELLING

Antacids were labelled with \(^{99}\)Tc using a pyrophosphate bridge as follows:

(a) Preparation of \(^{99}\)Tc-pyrophosphate: 30 mCi \(^{99}\)Tc-pertechnetate with a total volume of 5 ml was added to a vial containing 15 ml sodium pyrophosphate-H2O and 2 mg SnCl2.H2O in lyophilised form (Pyrotec, Sorin). This volume was adjusted with 0-15 M NaCl. After gentle mixing the solution was allowed to stand at room temperature for at least 5 minutes.

(b) Preparation of the \(^{99}\)Tc-pyrophosphate antacid: 10 ml of the antacid, magaldrate or Maalox, was put in a glass vial; 0-5 ml of the \(^{99}\)Tc-pyrophosphate was added drop by drop to the antacid. The resulting suspension was gently mixed with a 1 ml pipette and left to stand at room temperature for 5 minutes. After labelling we found that over 98% of the \(^{99}\)Tc was finally in \(^{99}\)Tc-pyrophosphate antacid form.

The stability of the \(^{99}\)Tc-pyrophosphate antacids in gastric juice was tested as follows: 0-2 ml of labelled antacid was added to 2 ml of gastric juice adjusted to a pH of 1-5 to pH 7 and incubated at 37°C for 10, 30, 60, and 120 minutes. After incubation the \(^{99}\)Tc-pyrophosphate antacids present were measured by centrifuging at 1000 g for 10 minutes. The solid phase in the bottom was separated from the liquid supernatant and both counted in a gammacounter.

The antacid capacity of the labelled antacids was compared with that of the unlabelled antacids as follows: 2 ml of antacid (unlabelled or labelled) was added by continuous stirring to a flask containing 10 ml of 0-4 M HCl and 10 ml of 0-15 M NaCl. The pH was measured with a pH meter and the time necessary to reach pH 3-4, 3-5, and 3-6 recorded. To ascertain whether the labelling of the antacids would alter protein binding, the following experiment was done: to 0-5 ml of antacid 10 μl of \(^{1}\)H-HSA (2 μg human
TABLE I  Percentage of radioactivity bound to magaldrate and Maalox in contact gastric juice at pH 1·5–7 at different times (n=3; mean (SD))

<table>
<thead>
<tr>
<th>pH</th>
<th>Time (min)</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Magaldrate</td>
<td>10</td>
<td>30</td>
<td>60</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maalox</td>
<td>10</td>
<td>30</td>
<td>60</td>
<td>120</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>pH</th>
<th>Magaldrate</th>
<th>10</th>
<th>30</th>
<th>60</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maalox</td>
<td>10</td>
<td>30</td>
<td>60</td>
<td>120</td>
</tr>
</tbody>
</table>

Serum albumin was added and incubated at 37°C for 5 minutes, and 2 ml of NaCl 0·9% was added and then centrifuged at 1000 g for 5 minutes. The acidity of the solid and liquid phases was measured.

To assess whether the labelling procedure might induce changes in the size of the colloidal particles and the formation of macroaggregates of the antacids, dark field microscopy of the labelled and unlabelled antacids was performed.

PROCEDURE
After an eight hour fast each subject ingested a meal consisting of a one egg omelette sandwich (50 g bread, 50 g egg, and 5 g olive oil) and 200 ml of orange juice. The total energy content of the meal was 957·7 MJ (400 kcal) (carbohydrate 40%, fat 30%, protein 22%).

One hour after the meal each subject ingested 10 ml of one of the two antacids previously labelled with 99mTc and was immediately placed in front of a camera detector (large view field camera on line to a standard computer. General Electric Maxi II on line to a PDP 11–34 Digital-Gamma 11.). The amount of radioactivity retained in the stomach was recorded in anterior and posterior projections (to calculate geometrical means).

These readings were repeated at six intervals of 15 minutes. During the study subjects could remain seated or walk about in a 5 metre area. All studies were done in the afternoon. Six smokers were not allowed to smoke for eight hours before the study. The study was repeated one week later under the same conditions with the other labelled antacid.

TABLE II  Antacid capacity of labelled antacids. With continuous stirring 10 ml of 0·15 M NaCl, 10 ml of 0·4 M HCl, and 2 ml of antacid (unlabelled or labelled) were added to a flask. Time intervals in seconds to reach fixed pH were recorded (mean (SD))

<table>
<thead>
<tr>
<th>pH</th>
<th>3·4</th>
<th>3·5</th>
<th>3·6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=5)</td>
<td>(n=5)</td>
<td>(n=5)</td>
</tr>
<tr>
<td>Magaldrate</td>
<td>13 (1·0)</td>
<td>25 (1·5)</td>
<td>30 (2·0)</td>
</tr>
<tr>
<td>99mTc magaldrate</td>
<td>15 (1·3)</td>
<td>25 (1·5)</td>
<td>30 (2·0)</td>
</tr>
<tr>
<td>Maalox</td>
<td>56 (3·0)</td>
<td>61 (3·6)</td>
<td>68 (4·3)</td>
</tr>
<tr>
<td>99mTc Maalox</td>
<td>57 (2·9)</td>
<td>59 (3·6)</td>
<td>65 (4·5)</td>
</tr>
</tbody>
</table>

Results

LABELLING OF ANTACIDS
The stability of the 99mTc-pyrophosphate antacids in gastric juice is shown in Table I. The percentage of radioactivity bound to magaldrate was greater than 96% at a pH of 1·5–7. The percentage of radioactivity bound to Maalox was slightly less, especially at 120 minutes at pH 1·5. But these results could be considered satisfactory for both antacids.

The antacid capacity of the labelled antacids compared with that of the unlabelled antacids is given in Table II. There were no significant differences between labelled and unlabelled antacids in the time needed to achieve a neutral pH.

Protein binding of both labelled and unlabelled magaldrate and Maalox showed a similar behaviour: mean (SD) labelled magaldrate 98·1 (0·1)%, unlabelled magaldrate 98·6 (0·1)% (n=5, not significant); labelled Maalox 78·5 (0·7)%, unlabelled Maalox 78·9 (0·6)% (n=5, not significant).

Dark field microscopy showed no macroaggregates in either labelled or unlabelled antacids, and the particulate size was about 0·5 μm for Maalox and 2–7 μm for magaldrate.
Gastric emptying of two radiolabelled antacids

GASTRIC EMPTYING OF ANTACIDS

The mean (SD) percentages of the antacids retained in the stomach fit a linear model. The t1/2 for magaldrate was 86.8 (15.3) minutes and for Maalox 52.3 (5.2) minutes (p<0.05).

The mean percentage of retention at the six times studied for each antacid is given in Table III. One hour after ingestion 58.4% of the magaldrate and 43.8% of the Maalox were retained in the stomach. After one and a half hours, the mean percentages were 41.2% and 28.2% respectively. Maalox emptied significantly faster at all times studied (p<0.01 at 15 and 30 minutes, p<0.02 at 45, 60, 75, and 90 minutes; Figure).

Discussion

Some antacids, especially those containing aluminium, delay gastric emptying of both liquids72 and solids.73 Aluminium ion, made soluble when aluminium hydroxide reacts with the hydrochloric acid in gastric contents, has been shown to inhibit acetylcholine induced contractions of rodent and human gastric smooth muscle.74 It must, however, be in contact with the gastric mucosa for one to two hours for aluminium ions to diffuse through to the muscle and inhibit contraction.75 Therefore, a prolonged period of antacid retention in the stomach may be considered desirable because rapid gastric emptying of liquid antacids is believed to be a limiting factor in the duration of their neutralising and cytoprotective effects.

Radionuclide imaging techniques are well established for monitoring gastric emptying.21 25 26 In studies on gastric emptying of labelled antacids for accurate results it is essential that the isotope remains associated with the components of antacids.

Ideally, the antacid should be radiolabelled with an isotope of one of its components, but none of the elements is currently available as a radioactive isotope for use in humans. In this study labelling was carried out with 99mTc. The labelled antacids had a satisfactory stability at a wide range of pH values (pH 1–5–7). The protein binding capacity of the antacids did not change after labelling, and we were able to show by darkfield microscopy that labelling antacids does not lead to the formation of macroaggregates which might show an emptying pattern different from that of the unlabelled antacids. The antacid capacity was similar in labelled and unlabelled samples.111 In has been used in all studies of gastric emptying of antacids carried out so far.27 28 Using 99mTc, which we have shown to be reliable, has advantages such as better physical properties for accurate detection, less radiation delivered to patients, and lower costs.

The meal given in this study had been evaluated in gastric emptying of solids and liquids in control subjects and under different physiological and pathological conditions.29 30 In addition, antacids were administered in the usual form one hour after the meal.

As there are notable differences in the methods used in published studies of gastric emptying of antacids, it is difficult to compare them. Jenkins et al studied emptying four hours after the meal27 and May et al 30 minutes after a liquid calorie meal.28

In this study at all time intervals the emptying of magaldrate was significantly slower than that of Maalox. This might have been due to the special chemical structure of magaldrate, to its ability to adhere to the stomach wall, or to its different capacity for binding proteins. Thus, in practice magaldrate performs as a solid in so much as gastric emptying is concerned (mean (SD) t1/2 magaldrate 86.8 (15.3) minutes; t1/2 for solid phase 85.3 (4.5) minutes). Theoretically, this slower gastric emptying should provide greater neutralising and cytoprotective effects. But Maalox, with a t1/2 of 52.3 (5.2) minutes, shows a rate of emptying similar to that found for a caloric liquid (Clinifeed ISO, Roussel Laboratories, Wembley Park, UK).30

99mTc labelling of antacids containing Al(OH)3 and Mg(OH)2 is feasible, stability is satisfactory, and gastric emptying of labelled antacids can be monitored by scintigraphic techniques. Therefore, gastric emptying of labelled antacids may be useful in monitoring how long antacids remain in patients’ stomachs.

This work was supported in part by grant FISS 88/0083 and in part by Roehring-Mannheim Laboratories.
Gastric emptying of two radiolabelled antacids.

J Monés, I Carrió, M Roca, M Estorch, R Calabuig, S Sainz, C Martinez-Duncker and F Vilardell

Gut 1991 32: 147-150
doi: 10.1136/gut.32.2.147

Updated information and services can be found at:
http://gut.bmj.com/content/32/2/147

Email alerting service

These include:
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

- Drugs: gastrointestinal system (207)
- Stomach and duodenum (1689)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/