Comparative study of four antacids

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Summary

Four antacid preparations have been studied in a stratified, randomized, double-blind trial to evaluate criteria which determine patients' acceptance of this type of therapy. There was a considerable range of judgements about palatability, but preference was determined not only by factors such as the smell, taste, texture and after-taste of the preparation, but also by the order in which the antacids were tested and by the age and sex of the patient. The preparations also differed considerably in acid-neutralizing capacity and ability to bind bile salts, as well as cost. We conclude that individuals requiring antacid therapy should be allowed to choose from among a range of preparations, in order to maximize compliance.

KEY WORDS: oesophagitis, duodenal ulcer, gastric ulcer.

Introduction

With the advent and therapeutic efficacy of potent inhibitors of gastric secretion, the role of antacids in the treatment of peptic ulcers has become less important (Morris and Rhodes, 1979; Editorial, 1981). However, antacids remain very useful for treating oesophagitis and less well-defined causes of dyspepsia (De Carlo, 1978; Graham, Smith and Patterson, 1983). The choice of antacids is wide—the British National Formulary lists 33 different preparations. The present study was undertaken in order to define some criteria for the selection of antacids, by comparing 4 commonly used preparations which represent the range of effects considered desirable for the treatment of oesophagitis. In a randomized, double-blind study, we tested aspects of the acceptability of the antacids to the patients, and measured the *in vitro* acid-neutralizing and bile salt-binding

capacities. We also considered the cost of each preparation.

Methods

Sixty consecutive patients (36 males and 24 females; mean age 48 years (range 21–76 years)) were recruited as volunteers from a gastroenterological out-patient clinic. The patients suffered from peptic diseases, including duodenal or gastric ulcer and oesophagitis.

TABLE 1. Antacids and ingredients

Code	Name	Manufacturer	Contents
A	Malinal	A. H. Robins	Almasilate (aluminium magnesium silicate)
B	Asilone	Berk	Dimethicone Aluminium hydroxide Magnesium oxide
C	Gaviscon	Reckitt & Colman	Sodium bicarbonate Sodium alginate
D	Maalox	Rorer	Aluminium hydroxide Magnesium hydroxide

The 4 antacids studied (Table 1) were placed in identical plain bottles and labelled A, B, C and D. The identity of the preparations was not known by either investigator or patient. Ten millilitres of each antacid were presented to each individual in a balanced, randomized order to ensure that each antacid was evaluated first on 15 occasions. Subjects performed the assessment in a manner analogous to wine-tasting and were asked to 'sniff, sip and savour' the preparation and subsequently to gargle, without swallowing. Following expectoration of the antacid, patients were asked to grade each of four criteria—aroma, flavour, texture and after-taste—as 'pleasant', 'acceptable', or 'unpleasant' and then to

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rank the preparations in order of preference for each criterion, with the most popular preparation being given a value of 4 and the least popular a value of 1. After each preparation had been tested and assessed, the mouth was rinsed with warm water until there was no residual taste and the procedure was repeated with each one of the other three preparations.

Sums of individual judgements for each criterion were used to determine overall palatability. To determine overall order of preference, scores for each criterion were summed. Statistical comparisons were made on absolute numbers using the χ^2 test. Rank correlation was assessed using the Wilcoxon and Mann-Whitney 'U'-tests. A *P* value of <0.05 was taken as being statistically significant.

To determine whether there were any specific age- or sex-related differences in patients' acceptance or preference for antacids, the patients were subdivided for the purpose of analysis into four groups: males older or younger than 50 years ($n=17$ and 19 , respectively) and females subdivided similarly ($n=12$ in each group).

Acid-neutralizing capacity was measured by the method of Fordtran, Morawski and Richardson (1973). Bile salt-binding capacity was measured by adding 0.33 ml of antacid to 5 ml of a solution of sodium taurocholate (10 mmol/litre). The pH was adjusted to 4.0 with 0.1 mol/litre hydrochloric acid. The suspension and control tubes (containing sodium taurocholate without antacid) were incubated at 37°C for 60 min and then centrifuged. The bile salt concentration in the supernatant was determined with 3- α -hydroxy-steroid dehydrogenase in kit form (Sterognost-3 α -Pho; Nyegaard and Co., Oslo, Norway) and spectrophotometry.

The cost of equivalent amounts of each preparation was derived from MIMS (Monthly Index of Medical Specialities, July 1983) or, when not available, from the manufacturer.

Results

Palatability (Fig. 1)

There were no differences among the four antacids regarding aroma. Two-thirds of the patients considered this to be 'pleasant' or 'acceptable' for each of the four preparations. There was greater variation among the antacids from the point of view of taste, texture and after-taste. More than half the patients considered that antacid C had an 'unpleasant' taste and texture, a proportion that was significantly higher than for preparations A, B and D ($P<0.01$). The majority of patients (82%) considered preparation D to be 'pleasant' or 'acceptable' to taste, while antacid B was considered by almost all patients (91%) to have a 'pleasant' or 'acceptable' after-taste, but

these proportions were not significantly different from the other antacids.

When scores for all four criteria were pooled to produce an index of overall palatability, there was no difference in results from antacids A, B and D. About one-quarter of the patients considered each to be 'unpleasant'. Nearly half the patients concluded that the overall palatability of antacid C was 'unpleasant', a proportion which was significantly higher than for the other three antacids ($P<0.01$).

Preference (Table 2)

Antacid B was the preferred preparation for three criteria, including taste ($P=\text{n.s.}$), texture ($P<0.02$) and after-taste ($P<0.02$). Antacid C was the least popular for these criteria ($P<0.01$ for taste and texture).

When preference scores for each of the four criteria were pooled, antacid B was preferred to antacids A and D (which were ranked equally). Antacid C was considered to be significantly less pleasant than the other three antacids ($P<0.01$).

TABLE 2. Order of preference of antacid preparations

Aroma	A : D : C : B
Taste	B : D : A $\gg$ C
Texture	B $>$ D : A $\gg$ C
Aftertaste	B $>$ A : D : C
All-round palatability	B $>$ A : D $\gg$ C

:Difference not statistically significant.

$>$ Difference significant $P<0.02$.

$\gg$ Difference significant $P<0.01$.

Order of sampling

Comparison of the palatability scores when each antacid was tasted first or last showed that for all preparations, all criteria were considered more pleasant when the preparation was sampled first than when sampled last. The proportion of 'pleasant' judgements was about twice as great when antacids were tasted first than when tasted last ($P<0.01$). The proportion of 'unpleasant' judgements on tasting last did not increase significantly for antacids A, B and D but there was a marked increase in the conclusion of 'unpleasant' for antacid C ($P<0.01$).

Order of sampling also affected the order of preference of each of the preparations. This effect was so marked that antacids tasted first were invariably ranked first in order of overall preference.

Age- and sex-related differences in judgement

There was no significant difference between the different age and sex groups for order of preference

for the antacids. However, there were differences between groups in their judgement of palatability. Males over the age of 50 were more likely to give antacid D a rating of 'pleasant' or 'acceptable' than other groups ($P<0.01$). Males (of all ages) gave antacid C more 'unpleasant' ratings than did females ($P<0.05$).

Among age-related differences, we noted that patients under the age of 50 years (male and female) were more likely to regard antacid B as being pleasant than were patients older than 50 ($P<0.02$), while male patients older than 50 considered antacid A to taste significantly better ($P<0.02$) than women

less than 50 years old. The latter, however, preferred the smell, taste and after-taste of antacid C significantly more than men older than 50 ($P<0.02$).

Acid-neutralizing capacity

The antacids showed a 4-fold range of buffering capacity, so that 10 ml of antacid buffered from 96 to 350 ml gastric juice containing 100 mmol/litre of hydrochloric acid (Table 3).

Bile acid-binding capacity

The four preparations were all reasonably potent

FIG. 1. Percentage of subjects expressing opinion about specified criteria of palatability. Densely dotted blocks indicate % of verdicts 'pleasant'; open blocks indicate verdict of 'acceptable'; lightly dotted blocks show percentage of verdicts of 'unpleasant' or 'nauseating'. A, B, C and D refer to antacid preparations.

TABLE 3. Acid-neutralizing capacity, bile salt-binding capacity and cost

Antacid	mmol HCl buffered by 10 ml of antacid	Percentage of bile salt removed from solution	Cost per 10 ml	Cost to buffer 100 mmol HCl
Malinal	167	42.8%	7.5p	4.5p
Asilone	350	52.1%	8.7p	2.5p
Gaviscon	96	47.1%	5.7p	5.9p
Maalox	257	62.2%	5.5p	2.1p

at binding bile salts from solution, with 40–60% of bile salts being removed with the solution at a pH of 4 (Table 3).

Cost

For equivalent volumes of antacids, there was a 50% difference in cost between the cheapest and most expensive products. When allowance was made for equivalent buffering capacities, the cost was lowest for preparation D (Table 3).

Discussion

In the present study, we tested four antacids with a wide range of composition, embracing most of the components found in other antacid preparations. The study confirmed personal and clinical impressions that antacid preparations are liked by only a minority of patients, tolerated by about three-quarters and found to be unpleasant or nauseating by the remaining 20–30%.

The study also showed that there was a change in the patients' attitudes towards the antacids during the course of each tasting session. Antacids tasted first were considered more palatable and given greater preference scores than those tasted last, an effect which might be attributable either to loss of enthusiasm caused by fatigue, or greater discrimination during tasting. The former seems more likely since, although there was a reduction in 'pleasant' considerations when antacids were tasted last, there was no proportional increase in the judgement of 'unpleasant' (except for preparation C). It seems, therefore, that enthusiasm waned somewhat during the course of the sampling session but was replaced by acceptance rather than rejection. We assume that if discriminative ability had increased during repeated testing, order of preference would have been less dependent on order of sampling, even though judgements about palatability may have changed. It is important, therefore, when designing studies such as the present, to balance the randomization of sampling of the preparations, so that the effects of the order of sampling are minimized.

One of the interesting findings of this study relates to the differences in preferences between sexes and in different age groups. Age- and sex-related differences in the appreciation of taste have been described previously. For example, young adults were found to be capable of discriminating lower concentrations of chemicals such as citric acid and caffeine, and reacted more strongly to suprathreshold concentrations, than did old people. The differences were particularly marked between young women and old men (as in some aspects of the present study). The authors concluded that 'age and gender are major factors in sour and bitter perception' (Hyde and

Feller, 1981). Similarly, differences between young and old test subjects were noted in the appreciation not only of taste characteristics such as sweetness, but also in the preference for aspects of texture such as smoothness (of puréed foods) (Stevens and Lawless, 1981). Just as the present study has found differences in the appreciation of antacid preparations, age- and sex-related differences in palatability have previously been described in a study of colloidal bulk-forming agents used in the treatment of diverticular disease and irritable bowel syndrome (Flaherty, O'Doherty and Fielding, 1980). We consider that the differences in the preference for antacid preparations between young and old, male and female, must be kept in mind by clinicians when using the preparations and by manufacturers when designing new ones, in order to maximize patient acceptance of the therapy.

The treatment of oesophagitis remains unsatisfactory, either because the objectives of treatment are not being achieved or because the objectives are wrong. Oesophagitis has been attributed to reflux of both acid gastric juice and of alkaline duodenal contents from the stomach into the oesophagus (Dodds *et al.*, 1981; Teillum, 1982) and failure of satisfactory treatment may be attributable to our present inability to control and negate both of these noxious factors. Antacid preparations are capable of buffering acid, adsorbing and inactivating pepsin and adsorbing or precipitating bile salts (Holm and Berstad, 1976; Malagelada and Carlson, 1979). It may be that our present therapeutic difficulties with oesophagitis are attributable to failure to supply sufficient amounts of antacids, sufficiently often, to provide sustained protection of the oesophageal mucosa. In this connection, the wide range of buffering capacities of the preparations and the ability to remove bile salts from solution do not correlate with the cost or palatability of the preparations and, therefore, with what are presumably determinants of patient compliance. Assuming that the four selected preparations represent most of the desirable properties of the available spectrum of preparations, it does not seem possible at present to recommend any one preparation for all-round theoretical and practical superiority over the other preparations. The more so, since other properties may be necessary to heal, and prevent the recurrence of, oesophagitis. For example, preparation C has been designed not primarily as an antacid, but to provide an alkaline alginate 'raft', which floats on the gastric contents and decreases gastro-oesophageal reflux (Stanciu and Bennett, 1974). We have not been able to test and assess, and therefore to compare, this attribute of the preparations.

In general, it may not matter very much which antacid preparation is used by patients, provided that treatment is acceptable and, consequently, carried

out. We have shown that the wide spectrum of individual tastes is reflected by the considerable range of subjective responses to the different criteria of palatability of the antacids. We conclude that patients who require treatment with an antacid should be allowed to choose between the many different preparations, since a verdict of 'palatable' and 'pleasant' seems most likely to ensure therapeutic compliance.

Acknowledgments

We wish to thank Dr J. S. Templeton (A. H. Robins Co., Ltd) Dr D. L. Williams (Reckitt & Colman Products Ltd) and Dr J. K. Butler (William H Rorer Inc.) for valuable comments.

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(Accepted 28 March 1984)