Acidity of gastric contents during nocturnal intragastric drip therapy in patients with duodenal ulcer¹

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EDITORIAL SYNOPSIS This report shows that an intragastric milk drip alone has a poor antacid action upon the nocturnal gastric secretion in duodenal ulcer patients. Milk containing 20 g. of sodium bicarbonate per litre is more effective and superior to a chelated aluminium compound, Glymaxil, given in 5% or 10% solution. About three-quarters of the gastric samples from the milk-bicarbonate trial were less acid than pH 4.

The acidity of the gastric contents in patients with duodenal ulcer tends to be greater than normal and to reach its maximum at night (James and Pickering, 1949). During waking hours, patients can reduce the acidity by taking frequent doses of antacid. To reduce nocturnal acidity, Winkelstein (1932) introduced intragastric drip therapy, using a solution of sodium bicarbonate in milk. Price and Sanderson (1956) showed that very large amounts of sodium bicarbonate must be given in this way to achieve complete neutralization of the gastric contents, and with these doses systemic alkalosis occurs (van Goidsenhoven, Gray, Price, and Sanderson, 1954). Poorly absorbed antacids have been given by continuous drip, notably aluminium hydroxide and aluminium phosphate, both of which are viscous and require special apparatus (Cornell and Hollander, 1942), and magnesium bicarbonate (Clark, 1950a), which is laxative. A recently introduced chelated aluminium compound, sodium gluconatodihydroxo-aluminate III (Glymaxil), can be administered easily and is said to be poorly absorbed.

Milk alone is sometimes administered by intragastric drip to patients with duodenal ulcer. No study has been made of its effect on the acidity of the gastric contents as compared to an inert control solution. The present study compares the effects of milk, milk and sodium bicarbonate, Glymaxil in two concentrations, and a control solution on the acidity of the gastric contents at night in patients with duodenal ulcer. This investigation has been limited to the effectiveness of these liquids as antacids;

possible metabolic effects and therapeutic benefits have not been studied.

METHOD

The acidity of the gastric contents of 15 patients with a radiologically proven uncomplicated duodenal ulcer was studied by a sampling technique on five nights between 10 p.m. and 6 a.m. Details of the patients' age and sex and of the results of gastric function tests are shown in Table I. The samples were obtained through a fine (10 Fr) radio-opaque nasogastric tube placed fluoroscopically so that the aspiration holes lay in the likely position of the gastric antrum. Before each sample was aspirated, 20 ml. of air was injected down the tube to clear it and to agitate the gastric contents around its tip; after each sample had been withdrawn, 10 ml. of water was injected down the tube to flush its lumen. Aspiration in this way was performed hourly on the hour between 10 p.m. and 6 a.m. by the nursing staff, who were instructed in the technique, and supervised during the early hours of the night by one of the authors. Each morning the samples were stored in a refrigerator until their pH was measured with a sealed glass electrode.

A different test liquid was given on each of the five nights through a fine rubber tube tied to the sampling tube, the tip of the drip tube being 25 cm. proximal to the tip of the sampling tube. The order of administration of the test liquids was varied from patient to patient in a Latin-square pattern. The liquids tested were:

(1) Control solution: 5% dextrose coloured with an inert green dye to resemble the Glymaxil solutions; (2) milk; (3) milk containing 20 g. of sodium bicarbonate per litre; (4) Glymaxil, 5% of the proprietary preparation by volume in water, containing 20 g. of the aluminium compound (and 20 g. of sucrose) per litre; (5) Glymaxil, 10% of the proprietary preparation by volume in water, containing 40 g. of the aluminium compound (and 40 g. of sucrose) per litre.

¹ This work was included in a thesis submitted by one of the authors (J.E.L.-J.) to the University of Cambridge for the degree of M.D.

TABLE I
DETAILS OF THE AGE, SEX, RESULTS OF GASTRIC SECRETORY STUDIES,
AND THE ACIDITY OF GASTRIC SAMPLES FOR EACH PATIENT

Patient	Sex	Age (yr.)	Secretion (mEq. HCl)			Uropepsinogen ⁴ (units/24 hr.)		No. of Samples (pH ≤ 2.0)				
			Basal ¹	M.A.O. ²	P.A.O. ³			Control	Milk	5% g. Glymaxil	10% g. Glymaxil	Milk + Bicarbonate
1	M	49	2.3	44.1	23.7	422	480	7	6	4	0	3
2	M	41	6.6	27.0	16.1	93	124	7	3	1	0	2
3	M	36	8.3	35.2	27.5	331	403	5	1	5	2	1
4	F	42	3.1	31.2	16.7	366	76	8	5	1	1	2
5	M	53	0.8	28.7	15.2	264	247	2	1	0	0	0
6	M	43	2.2	28.9	16.8	—	—	5	7	3	1	3
7	F	50	0.7	23.7	13.9	174	408	4	0	2	1	0
8	M	37	2.8	37.7	24.6	664	663	7	7	2	2	4
9	M	29	1.2	34.8	19.6	—	—	5	5	2	2	0
10	M	61	1.3	33.2	19.4	168	132	7	2	0	0	0
11	M	42	0.5	39.0	22.6	180	153	7	5	3	0	1
12	M	36	4.0	36.7	20.6	347	585	7	5	2	3	1
13	M	29	14.9	35.4	19.4	343	306	7	2	2	1	1
14	F	68	0.1	21.5	12.5	132	122	0	0	0	0	1
15	M	52	0.4	—	—	330	304	6	2	1	0	0

¹One hour unstimulated secretion
²M.A.O. = one hour after histamine acid phosphate 0.04 mg./kg. body weight
³P.A.O. = peak half-hour after histamine acid phosphate 0.04 mg./kg. body weight
⁴Two 24-hour urine specimens estimated by a modification of the method of Sircus (1954)
Normal values for men = 144 ± 79 units/24 hr.
Normal values for women = 95 ± 52 units/24 hr.

The patients took a normal ward diet during the day and a milk drink during the evening. A control sample was aspirated at 10 p.m. and a hypnotic was then given. No other drugs, no alkalis, and no food were taken during the test periods. One litre of a test liquid was given each night by continuous intragastric drip between 10 p.m. and 6 a.m. The total volume was divided into two portions of 500 ml., one to be given between 10 p.m. and 2 a.m. and the other to be given between 2 a.m. and 6 a.m. The nurses were encouraged to adjust the speed of the drip from time to time so that the test liquid was given at a steady rate.

RESULTS

TITRATION IN VITRO The results of titrating 10 ml. of each of the test liquids against 0.1 N HCl are

FIG. 1. Results of titration in vitro of the test liquids with 0.1 N HCl.

shown in Figure 1. The buffering power of the test liquids was found to increase in the order, control solution < milk < 5% Glymaxil < 10% Glymaxil < milk and bicarbonate.

FIG. 2. Cumulative diagram showing the proportion of gastric samples less acid than a given pH for each of the test liquids.

ACIDITY OF THE GASTRIC SAMPLES The results for all the patients have been pooled so that for each test liquid a maximum of 120 samples is available for

analysis. The frequency with which samples of different acidity were found with each treatment is shown graphically in Fig. 2, a cumulative diagram which shows the proportion of samples less acid than any given pH. These curves are similar in sequence to those obtained by titration of the test liquids *in vitro*. The proportion of samples of low acidity tends to increase progressively in the order, control solution < milk, < 5% Glymaxil < 10% Glymaxil < milk and bicarbonate. Over 60% of the samples with milk and bicarbonate were less acid than pH 6.5. Only 28% of the samples were less acid than pH 2 during administration of the control solution compared with 57% with milk and over 75% with the other solutions.

The same results are shown in a different form in Table II, in which the number of samples in different pH ranges are set out. As one passes down the table the proportion of samples more acid than pH 4 decreases and the proportion less acid than pH 4 increases.

TABLE II

DISTRIBUTION OF SAMPLES IN DIFFERENT pH RANGES

	No. of Samples in Different pH Ranges					Total
	≤1.5	1.6-2	2.1-4	4.1-6	>6	
Control	21	63	26	2	5	117
Milk	13	38	46	20	1	118
5% Glymaxil	6	22	48	28	16	120
10% Glymaxil	3	10	38	42	25	118
Milk + bicarbonate	8	11	12	16	73	120

The results have also been assessed by considering the solutions in pairs and subtracting the values for the corresponding samples at each hour of the night for each patient. The mean of these differences over the two nights for each patient has been calculated. From the mean difference for each patient, the mean difference for all the patients has been determined and the significance assessed by Student's *t* test (Table III). The mean shows a significant departure from zero ($P < 0.01$) in every case.

TABLE III

MEAN DIFFERENCES BETWEEN SAMPLES TAKEN AT CORRESPONDING TIMES IN THE SAME PATIENT FOR THE FIVE TEST LIQUIDS TAKEN IN PAIRS

Test Liquid		Differences Mean (S.E.)	P ¹ (n = 14)
A Control	B-A	+0.64 (±0.20)	<0.01
B Milk	C-B	+0.96 (±0.22)	<0.001
C 5% Glymaxil	D-C	+0.69 (±0.21)	<0.01
D 10% Glymaxil	E-D	+0.86 (±0.24)	<0.01
E Milk and bicarbonate			

¹The probability that these differences represent a real departure from zero is shown.

FIG. 3. The number of specimens less acid than pH 4 at each hour of the night for each of the test liquids (maximum number = 15).

CHANGES IN ACIDITY FROM HOUR TO HOUR DURING THE NIGHT The number of specimens less acid than pH 4 at each hour of the night is shown in Figure 3. With each test liquid, the number of samples of low acidity tended to increase as the hours passed. No more than two out of the possible 15 samples were less acid than pH 4 at any hour with the control solution, whereas with milk and sodium bicarbonate 12 to 14 of the possible 15 samples were less acid than pH 4 between 1 and 6 a.m.

COMPARISON OF THE RESULTS OBTAINED WITH GASTRIC FUNCTION TESTS Results of gastric function tests performed on the patients are set out in Table I and are compared with the number of samples obtained of pH ≤ 2. No correlation is apparent.

DISCUSSION

Milk is widely used in the dietary treatment of duodenal ulcer. Douthwaite (1947) recommended a continuous intragastric drip of milk as a good method of neutralizing the gastric contents. However, in three patients with duodenal ulcer receiving this treatment, Douthwaite and Hunt (1950) found that 11 of 25 gastric samples were more acid than pH 1.5. From measurements of the chloride concentration in the samples they calculated that the patients were secreting 183, 194, and 350 ml. of gastric juice each hour, suggesting that the milk was acting as a stimulus to gastric secretion. Thus, although the buffering power of milk can be demonstrated *in vitro* (Freezer, Gibson, and Matthews, 1928), this effect might be outweighed by the stimulus which it provides to gastric secretion. The present results show that the acidity of the gastric contents is

reduced by 1 litre of milk given over eight hours.

Winkelstein (1932), when he introduced continuous intragastric drip therapy, used milk containing 5 g. of sodium bicarbonate in 1,200 ml. (one level teaspoon to the quart). With Cornell and Hollander (1942), he showed in a group of nine patients (eight duodenal ulcer, one gastric ulcer) receiving 1,200 ml. of this solution every eight hours, that 30.2% of gastric samples aspirated through the drip tube during the night were more acid than pH 2.0. Seeking to achieve almost complete neutralization, Doll *et al.* (1956) found in 15 patients with duodenal ulcer that 60 to 140 g. of sodium bicarbonate, dissolved in about 3 l. of milk, was needed to maintain the gastric contents at an acidity less than pH 4 throughout the 24 hours. This criterion is very strict and the present study was designed to test the effect of a smaller amount of sodium bicarbonate given at night only. The results have shown that with 20 g. of sodium bicarbonate, dissolved in one litre of milk, and given over eight hours, 19% of samples (mainly during the first two hours of the drip) were of high acidity (pH $\leq$ 2.0) and 73% were less acid than pH 6.

Sodium bicarbonate is thus an effective antacid but the large amounts needed tend to produce a metabolic alkalosis (van Goidsenhoven *et al.*, 1954). Poorly absorbed antacids have therefore been substituted. Woldman and Rowland (1936) gave aluminium hydroxide by continuous intragastric drip and it is almost as effective as milk containing 4 g. of sodium bicarbonate per litre (Cornell, Hollander, and Winkelstein, 1942). Most workers, however, have found it inconvenient to administer (Clark, 1950a) as the gel tends to sediment and block the drip tube even when a specially designed apparatus (Cornell and Hollander, 1942) is used. Aluminium phosphate is less viscous, is equally effective (Cornell *et al.*, 1942), and is less constipating. Clark (1950a) used a solution of magnesium bicarbonate but during this treatment 39% of gastric samples were more acid than pH 2 (Clark, 1950b).

The water-soluble chelated aluminium compound tested in this study proved to be a convenient and effective antacid. Using a 10% solution of the proprietary preparation (4 g. of aluminium compound per 100 ml.), 81% of samples were less acid than pH 3, compared with 76% with the milk and bicarbonate solution. The milk and bicarbonate solution was more effective than 10% Glymaxil in reducing the acidity to lower levels. A 5% solution of Glymaxil was a more effective antacid than milk alone. One patient in this series complained of diarrhoea during the administration of Glymaxil, and this side-effect has been noted occasionally in other patients.

No controlled therapeutic trial of antacid drip therapy for duodenal ulcer has been carried out. In patients with gastric ulcer, Doll *et al.* (1956) in a controlled trial found that an alkaline milk drip did not affect the healing rate. It is known, however, that duodenal ulcers tend to be associated with gastric hypersecretion of acid, whereas there is no such association with ulcers situated in the body of the stomach. The results of a trial of therapy for gastric ulcer do not therefore necessarily hold good for duodenal ulcer. It is commonly stated on theoretical grounds that, to be effective, a treatment for duodenal ulcer should reduce the acidity of the gastric contents to at least pH 3.5. Although the acidity, *i.e.*, the concentration of acid, of the gastric contents at night in patients with duodenal ulcer is significantly greater than in normal subjects (Watkinson, 1951), the increase is probably less than ten-fold. For example, Atkinson and Henley (1955) found that 74% of gastric samples obtained at night from their 15 patients with duodenal ulcer were more acid than pH 2 as compared with 56% of samples obtained from an equal number of subjects without gastrointestinal disease. It seems possible that a reduction of acidity to within the normal range could be beneficial. A controlled therapeutic trial of the effect of antacid therapy upon the healing and prognosis of duodenal ulcer is needed.

SUMMARY

The effect of four test liquids given by continuous intragastric drip on the acidity of the gastric contents at night has been compared with a control solution in 15 patients with duodenal ulcer.

Milk alone reduced the acidity of the gastric contents but was the least effective of the liquids tested, 18% of samples being less acid than pH 4 compared with 6% of samples with the control solution.

Milk containing 20 g. of sodium bicarbonate per litre was the most effective antacid tested, 74% of samples being less acid than pH 4.

A chelated aluminium compound, Glymaxil, given in two strengths as a solution containing 20 and 40 g. of the compound per litre (5 and 10% solutions of the proprietary preparation), gave intermediate results.

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