Simultaneous measurement of gastric acid and duodenal alkali secretion by in situ titration in health and disease

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SUMMARY We have devised a technique for simultaneously measuring the acid secretion into the stomach and alkali into the duodenum by in situ titration using a modification of the technique of Fordtran and Walsh. Using this technique, the results of acid and alkali secretion measured simultaneously were identical with those obtained using the conventional aspiration method on separate days. In response to stimulation with pentagastrin acid output was $17.2 \pm 1.4$ vs $15.4 \pm 1.9$ mmol/h and alkali response with secretin was $16.0 \pm 0.8$ vs $14.4 \pm 1.5$ mmol/h. The response to food was measured in 10 control subjects, 10 patients with duodenal ulcer, and 10 patients with pancreatitis. In controls, the acid and alkaline secretion were similar ($15.8 \pm 1.7$ vs $18.2 \pm 1.3$ mmol/h), in patients with duodenal ulcer acid secretion was significantly greater than alkaline secretion ($31.9 \pm 2.2$ vs $21.9 \pm 1.7$ mmol/h), and in patients with pancreatitis the alkali secretion was significantly less than acid ($19.8 \pm 1.9$ mmol/h acid vs $11.4 \pm 0.6$ mmol/h alkali). It can, therefore, be concluded that in response to food the patients with duodenal ulcer are significant hypersecretors of acid (DU acid > DU alkali output) and patients with pancreatitis are significant hyposecretors of alkali (pancreatitis–alkaline output < acid output) and normal subjects secrete equal amounts of acid and alkali.

Among the many unexplained facts about duodenal ulcer disease is the occurrence of the ulcer in the first part of the duodenum in the vast majority of cases. The most popular hypothesis suggests that the mucosa of the first part is the site where gastric acid is insufficiently neutralised by the alkaline secretion present. An ulcer thus forms depending on the balance between acid and alkali secretion. A high incidence of duodenal ulcer in patients with chronic pancreatitis has renewed an interest in the interactions between pancreatic and gastric secretion and speculation regarding the possible causes of the association between chronic pancreatitis and duodenal ulceration.

Duodenal defence mechanisms due to the action of food have not been studied extensively, probably because of the lack of knowledge about the rates of acid and alkali secreted during the normal course of digestion. Gastric acid and duodenal alkali secretion after food have been studied in animals by creating gastric and pancreatic fistulae. In man, studies of gastric acid and duodenal alkali secretion on the same subjects have been done on different days after histamine and secretin stimulation using the conventional aspiration techniques.

In 1973, Fordtran and Walsh described and validated a method of studying the gastric acid response to a meal by in situ titration. We have adapted this method to examine simultaneously, acid secretion into the stomach and alkaline secretion into the duodenum. We describe the conduct of the test, the results of an examination into its validity and the measurement of the simultaneous acid–alkali response to a standard meal in control subjects, patients with duodenal ulcer and patients with chronic pancreatitis.

Methods

Patients
The study was conducted on 40 patients. Twenty were control subjects without any gastrointestinal disease, 10 patients had duodenal ulcer proved by barium meal and endoscopy, and 10 patients had chronic pancreatitis. Patients with chronic pancreatitis were selected who had gross evidence of
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Date: All having epigastric pain, diabetes, and malabsorption. Six of them showed pancreatic calcification on radiograph.

Composition of the standard meal
Wheat chapatis 80 g; cooked potatoes 50 g; vegetable ghee 1 g; salt 1 g; and water 500 ml.

Conventional aspiration method
After an overnight fast, the patient was intubated with a double lumen Dreiling tube. The tip of the tube was positioned at the duodenojejunal flexure and this position was checked by fluoroscopy. Either gastric or duodenal contents were manually aspirated with a syringe at three minute intervals. The aspirates were divided into 15 minute fractions and collected for a ‘basal’ hour and one hour after intramuscular pentagastrin 8 μg/kg² or intravenous secretion (1 U/kg). The acidity of the gastric contents was estimated by titration against 0·1 sodium hydroxide solution to pH 7·0 and the alkalinity of the duodenal contents was measured by back titration using 0·1N HCl.

Simultaneous intragastric—intraduodenal titration
The fasting patient was intubated with the Dreiling tube. The resting juice was aspirated and discarded. Two millilitre samples of gastric and duodenal contents were aspirated separately after every three minutes, the pH measured and the samples returned to their respective compartments. The pH of gastric contents was maintained at 3·0 by infusing 0·3N sodium bicarbonate and that of the duodenal contents at 6·0 by adding 0·1N hydrochloric acid via the gastric and duodenal lumina. The standard diet was eaten. The acid and alkali responses to food were then measured. Finally, the gastric acid and duodenal alkali output after pentagastrin and secretin stimulation were estimated for the next four hours using this new technique to compare it with the conventional aspiration method. The amount of alkali or acid infused per hour to maintain the intragastric pH at 3·0 and the intraduodenal pH at 6·0 were considered to be equivalent to the amount of acid or alkali secreted into the stomach or duodenum per hour.

Calculations
Peak acid output = two highest consecutive 15 minute acid output values × 2. Peak alkali output = two highest consecutive 15 minute alkali output values × 2.

Statistical methods
The results are expressed as mean and standard error (M ± SE). The difference between the two groups were analysed using Student’s paired t test. A value of less than 0·05 was considered to be significant.

Results
Validity of the simultaneous intragastric—intraduodenal titration method assessed against the conventional aspiration technique
As shown in Figure 1, the peak acid output after pentagastrin by the conventional aspiration method was 15·4±1·9 mmol/h and by the simultaneous intragastric—intraduodenal titration technique it was 17·2±1·4 mmol/h. After an injection of secretin, the peak alkali output by conventional aspiration method was 14·4±1·5 mmol/h and by in situ titration was 16·0±0·8 mmol/h. The results showed no significant difference in the peak acid output after pentagastrin or peak alkali output after secretin whether these were measured by conventional aspiration or by in situ titration.

Simultaneous acid—alkali response to food in health and disease
Control subjects
In 10 control subjects, peak acid output to the standard meal was 15·9±1·7 mmol/h and the simultaneous alkali response (PBO) was 18·2±1·3 mmol/h. The difference between the acid and alkali output was not significant (Fig. 2).

Duodenal ulcer patients
The peak acid output to the meal in 10 duodenal ulcer patients was 31·9±2·2 mmol/h and alkali output was 21·9±1·7 mmol/h. The acid output was significantly higher than the alkali output in these patients (p<0·01).

Patients with chronic pancreatitis
In this group of 10 patients the meal stimulated acid response was 19·8±1·9 mmol/h. The alkali response to the meal was 11·4±0·6 mmol/h and was significantly lower than the acid output (p<0·05).

Fig. 1  Validity of intragastric—intraduodenal titration.
ACID Response to food in control subjects, patients with duodenal ulcer, and in patients with pancreatitis

The peak acid output after food in duodenal ulcer patients was significantly higher (31.9±2.2 mmol/h) than in control subjects (15.8±1.7 mmol/h) and was also higher than the acid response to food in patients with pancreatitis (19.8±1.9 mmol/h), p<0.05. There was no significant difference in peak acid output after food in control subjects and in patients with pancreatitis (p<0.05).

ALKALI response to food in control subjects, patients with duodenal ulcer, and in patients with pancreatitis

The peak alkali response to food in duodenal ulcer patients (21.9±1.7 mmol/h) was not significantly different (p<0.05) to that obtained in control subjects (18.2±1.3 mmol/h) but it was significantly higher than the alkaline response to food in patients with pancreatitis (11.4±0.6 mmol/h) (p<0.05).

Discussion

The gastric acid that enters the duodenal bulb from the stomach is continuously buffered and neutralised by duodenal bicarbonate. The resultant pH in the first part of the duodenum influences a number of physiological and pathological processes including gastric emptying,⁶ further secretion of acid,⁶ release of secretin,² and possibly the occurrence of duodenal ulceration.

The relationship between maximal gastric acid and pancreatic alkali secretion has been studied in dogs by creating gastric and pancreatic fistulae and it has been found that the maximal alkali output in the dog neutralises only one third of the maximal acid output.⁷ In man, the maximal gastric acid and alkali secretion into the stomach and duodenum has been measured on separate occasions by using either pentagastrin or secretin.⁸ In these human studies, acid secretion was found to be higher¹⁰ or equal⁵ to alkali secretion in patients with duodenal ulcer. There is evidence that a test meal may result in the same amount of acid secretion as does a maximally stimulating dose of histamine when this is measured by the rise in base excess in the arterial blood.⁸

Information is not available, however, in man on the meal stimulated gastric acid response and the duodenal alkali response measured simultaneously.

We have designed and validated a technique for making this possible by a modification of the in situ titration method of Fordtran and Walsh⁶ for measuring the gastric acid response to a steak meal. In our technique, we kept the intragastric pH at 3-0 by adding 0.3N sodium bicarbonate into the stomach and the intraduodenal pH at 6-0 by adding 0.1N hydrochloric acid into the duodenum.

Manipulation of the intragastric and intraduodenal pH may exert some 'non-physiological' effects. Firstly, by increasing the volume of gastric contents it may enhance gastric emptying and also augment gastrin release by the distension of the stomach. Similar changes in duodenal emptying and hormonal release may perhaps also occur after intraduodenal titration.

The conventional aspiration method, however, has its own disadvantages, being reliant on exogenous stimuli and involving continuous aspiration of gastric and duodenal secretions which normally are in prolonged contact with the gastric and duodenal mucosa. There is also a negative pressure in the stomach and duodenum and this may encourage alkali to reflux into the stomach as well as acid to empty from the stomach into the duodenum.⁹ In spite of the inaccuracies inherent in both systems, we found that the peak acid output to pentagastrin and peak bicarbonate output to secretin were very similar whether measured by conventional aspiration or by the in situ titration method. In these secretory studies, markers were not used so that the measurements of gastric and duodenal alkali made no allowance for their emptying and neutralisation. Berstad and Peterson,¹⁰ however, measured acid and alkali by using polyethylene glycol in the duodenum and the amount of reflux did not change their results to any significant degree. The advantages of our technique are that it can measure simultaneously the acid and alkali responses to a meal and can be completed in a day.

The results of using this technique on control subjects and patients with duodenal ulcer and pancreatitis were interesting though not entirely unexpected.
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The equivalent amount of acid–alkali secretion in control subjects seems to be understandable. A complete neutralisation of gastric acid probably occurs in a normal person after a meal. Other studies in man have suggested that the first part of duodenum maintains a neutral pH for most of the time during the digestion of a meal in healthy subjects whereas the pH is mainly acidic in patients with duodenal ulcer.

This relative acid hypersecretion in duodenal ulcer patients confirms what is generally believed but has not been shown by actual measurements after a meal. In patients with duodenal ulcer the alkali output was the same as that found in control subjects but this amounted to only two thirds of their ‘raised’ acid output. These results thus support the view that it is an excessive secretion of acid rather than a diminished secretion of alkali which is the pathogenic mechanism of duodenal ulcer disease.

When compared with control subjects, patients with chronic pancreatitis had a ‘normal’ acid output after a meal but this greatly exceeded the subnormal alkali response. The duodenum is thus again possibly subject to the action of an excess acid and this may also explain why patients with pancreatitis are more prone to develop duodenal ulcer.

This method of simultaneous measurement of gastric acid and duodenal alkali by in situ titration is probably valid and could be used with advantage in a number of other clinical situations.

References


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