Effect of pH changes on the cardiac sphincter

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SUMMARY In 16 normal subjects the pressure characteristics of the cardiac sphincter have been examined. The effect of perfusing the gastric aspect of the sphincter mucosa has been studied by comparing the effects of saline with those of solutions where pH ranged from 1.0 to 8.0. Acid perfusion produced an increase in sphincteric pressure, particularly at pH 3.0. This suggests that a physiological mechanism exists which can increase the barrier pressure to gastrooesophageal reflux during periods of active secretion of the stomach, as occurs in digestion.

The evidence in favour of a lower oesophageal sphincter now seems conclusive, though its exact role in the prevention of reflux is debated. There have been many studies of the nervous mechanism regulating the sphincter (Carlson, Boyd, and Percy, 1922; Fergusson, 1963; Clark and Vane, 1961; Carveth, Schlegel, Code, and Ellis, 1962; Greenwood, Schlegel, Code, and Ellis, 1962). There is little information, however, on the effects of stimuli applied locally to the cardia though Cannon (1908) showed that rhythmic activity of the cardia in the cat was increased by contact with hydrochloric acid. It seemed likely that acid might be a potent local stimulus, and the present study concerns the pressure changes recorded in the cardiac sphincter in response to perfusion of its gastric aspect of solutions of different pH. The results suggest that the sphincter responds to acid in a dynamic fashion designed to increase sphincteric pressure.

MATERIAL AND METHODS

Intraluminal pressures in the oesophagus and stomach were determined by a manometric technique modified from those previously described (Fyke, Code, and Schlegel, 1956; Atkinson, Edwards, Honour, and Rowlands, 1957). Two water-filled polythene tubes of internal diameter 1.2 mm were fastened together and sealed at their distal ends. Pressure measurements were made through a side hole in one of these tubes situated 5 cm from the tip, and this tube was connected via a strain gauge transducer (Statham PGA D300) to an amplified electromanometer, the deflections being recorded on moving photographic paper. Respiratory deflections were recorded simultaneously from a pneumograph strapped around the chest. The second polythene tube was used to perfuse the gastric mucosa just below the cardia through openings situated 3, 2, 1, and 0 cm from

the end (Fig. 1) using either normal saline or solutions of hydrochloric acid of varying concentration. The hydrostatic pressure of the perfusing fluid was adjusted so that it was just greater than the mean gastric pressure. The double-lumen tube was withdrawn in half-centimetre steps and pressure measurements were made at each step during at least five full respiratory cycles. During these pressure measurements perfusion of the gastric mucosa was carried out at a rate which did not exceed 15 ml/minute through the second tube. As the experiment progressed the upper side holes of the perfusion tube became occluded by the sphincter but perfusion continued through the lower holes, and so on until the whole sphincter profile had been obtained.

Studies were performed in 16 normal subjects with no previous history of dyspepsia and who were instructed not to eat or drink for at least six hours before examination. The double-lumen tube was swallowed with the subject erect, and thereafter tests were carried out in the supine position with the levels of the transducers adjusted to the mid-axillary line. In six subjects the sphincteric response was measured comparing perfusion with normal saline and perfusion with N/20 hydrochloric acid. In another group of five subjects a comparison was made of sphincteric responses to solutions of pH 1.5, 3.0, 6.0, and 8.0, the solutions being administered in random order. The final study in a further five normal subjects compared sphincteric responses to perfusion with solutions of pH 1.0, 2.0, 3.0, and 4.0. The pressure tracings obtained in all these experiments were measured using both end inspiratory and end expiratory excursions. The latter showed more consistent results and have been used in presenting the data. Zero pressure atmospheric was taken from the level of the transducer, and three recordings were obtained at each step, mean end expiratory pressure giving the best record.

RESULTS

Figure 2 is a typical tracing from one of the exper-

iments and indicates the type of response obtained. This shows the characteristic high pressure zone typical of the sphincter and straddling the diaphragmatic hiatus which is represented by the point at which there is reversal of the respiratory excursion. It can be seen that perfusion of the gastric mucosa with normal saline has little effect on sphincteric pressure whereas perfusion with N/20 hydrochloric acid produces a marked rise in pressure. From these tracings measurements of intragastric pressure, maximum sphincteric pressure, and oesophageal pressure can be obtained and the pressure gradient of the gastrooesophageal junction and the barrier pressure to reflux can be calculated.

Figure 3 illustrates the maximum sphincteric pressures obtained in six normal subjects during perfusion with saline. There was little response except in one subject where there was a rise of pressure measuring 2.5 cm H₂O. The effect of perfusion with N/20 hydrochloric acid, however, was to produce a distinct rise in sphincteric pressure in all but one of the subjects. The mean values of the pressure measurements are shown in Table I. There were minor changes in the intragastric pressures which were reflected in the gastrooesophageal gradient since intraoesophageal pressures did not alter. On

perfusion with acid the mean maximum sphincteric pressure rose from 11.8 ± 1.2 to 16.9 ± 1.6 cm H₂O, a significant alteration ($p < 0.05 > 0.02$), while the barrier pressure was also significantly altered from 6.8 ± 1.8 to 10.2 ± 1.4 cm H₂O ($p < 0.1$).

Figure 4 shows the maximum sphincteric pressures in five subjects when perfusion was performed with solutions of pH 1.5, 3.0, 6.0, and 8.0 given in random order. These have been compared with sphincteric pressures obtained immediately before perfusion and it can be seen that there are extremely variable results, the most consistent change being found with a solution of pH 1.5 where there was an increase in pressure in all except one subject. Table II shows the mean results derived from these studies, and it can be seen that the only changes are an increase in the mean barrier pressures produced by solutions of pH 3.0 and 1.5, but the results are not statistically significant.

The results of these studies, using solutions over a wide pH range, suggested that the greatest change in sphincteric pressures occurred with more acidic solutions. Therefore five further subjects were examined using perfusion of solutions at pH 1.0, 2.0, 3.0, and 4.0 given in random order. The results are

TABLE I

RESULTS IN FIVE SUBJECTS COMPARING MEAN PRESSURE CHANGES WITH STANDARD DEVIATION ON PERFUSION WITH SALINE AND ON PERFUSION WITH N/20 HYDROCHLORIC ACID

	Mean Gastric Pressure	Maximum Sphincter Pressure	Barrier Pressure to Reflux	Mean Oesophageal Pressure	Gastrooesophageal Gradient
Control	5.0 ± 1.0	11.8 ± 1.2	6.8 ± 1.8	1.0	4.1 ± 1.1
Saline perfusion	6.5 ± 1.0	11.7 ± 1.3	5.2 ± 1.3	0.5	5.3 ± 0.6
Acid perfusion N/20 HCl	6.5 ± 0.7	16.7 ± 1.6	10.2 ± 1.4	1.0	5.5 ± 0.7

TABLE II

RESULTS IN FIVE SUBJECTS COMPARING MEAN PRESSURE CHANGES WITH STANDARD DEVIATION ON PERFUSING WITH SOLUTIONS AT DIFFERENT pH LEVELS

pH of Solution	Mean Gastric Pressure	Maximum Sphincter Pressure	Barrier Pressure to Reflux	Mean Oesophageal Pressure	Gastrooesophageal Gradient
Control	5.7 ± 3.6	9.9 ± 2.9	4.2 ± 1.7	0.3	5.4 ± 1.1
8.0	5.6 ± 1.9	8.8 ± 1.5	3.1 ± 1.1	0.1	5.6 ± 1.7
6.0	4.2 ± 2.1	11.2 ± 3.3	5.3 ± 1.6	0.9	5.3 ± 1.9
3.0	6.7 ± 1.6	13.1 ± 1.8	6.4 ± 1.8	1.3	5.4 ± 1.2
1.5	6.3 ± 1.8	12.0 ± 1.4	5.7 ± 1.1	1.2	5.0 ± 1.1

TABLE III

RESULTS IN FIVE SUBJECTS COMPARING MEAN PRESSURE CHANGES WITH STANDARD DEVIATION ON PERFUSION WITH SOLUTIONS VARYING FROM pH 1.0 TO 4.0

pH of Solution	Mean Gastric Pressure	Maximum Sphincter Pressure	Barrier Pressure to Reflux	Mean Oesophageal Pressure	Gastrooesophageal Gradient
Control	4.2 ± 0.7	6.4 ± 1.2	2.2 ± 0.5	0.7	3.7 ± 0.7
1.0	4.9 ± 1.2	7.9 ± 0.8	3.0 ± 0.5	1.4	2.4 ± 0.8
2.0	4.5 ± 0.8	8.6 ± 1.3	4.1 ± 0.6	1.4	3.0 ± 0.8
3.0	4.4 ± 0.6	10.4 ± 1.0	6.0 ± 0.8	1.1	3.4 ± 0.5
4.0	4.1 ± 0.6	9.3 ± 1.0	5.2 ± 0.6	0.9	3.1 ± 0.5

FIG. 1

FIG. 2.

FIG. 3.

FIG. 1. The double-lumen tube allows for pressure measurements through one lumen and perfusion through the other.

FIG. 2. Sphincter profile tracings in the normal subject comparing the effect of saline and N/20 hydrochloric acid. The arrow indicates the diaphragmatic hiatus.

FIG. 3. Mean sphincter pressures under resting conditions (control) after perfusion with saline and acid.

FIG. 4. The effect of perfusing the gastric aspect of the cardiac sphincter with solutions of varying pH.

FIG. 4.

FIG. 5. The effect of perfusing the gastric aspect of the cardiac sphincter with solutions at pH 1.0–4.0.

shown in Fig. 5, when at pH 1.0 two of the five subjects showed an increase in sphincteric pressure compared with three subjects at pH 2.0. The most consistent changes were found at pH 3.0 where all five subjects showed an increase in sphincteric pressure, the mean rising from 6.4 ± 1.2 to 10.4 ± 1.0 cm H₂O. Perfusing with a solution at pH 4.0, the mean pressure rose to 9.3 ± 1.0 cm H₂O. Only the pressure change at pH 3.0 was statistically significant ($P < 0.01$). Table III summarizes the results of the experiments, and, apart from minor changes in intraoesophageal pressures, the most important change related to increase in barrier pressure, which was statistically significant both at pH 3.0 ($P < 0.01$) and at pH 4.0 ($P < 0.02$) but not for the other two solutions.

It seemed likely that the changes in sphincteric pressure were mediated through a local reflex and studies were performed before and after giving atropine. Figure 6 shows the results in three subjects where the response to acid perfusion at pH 3.0 was a rise from the mean of 10.2 to 12.3 cm H₂O. Atropine sulphate, 1.2 mg, was given intravenously and after 30 minutes the experiment was repeated. It can be seen that this resulted both in a reduction of the mean basal sphincteric pressures and abolition of the effect of acid perfusion.

DISCUSSION

The existence of a lower oesophageal sphincter in man has been clearly demonstrated as a zone of high pressure at the lower end of the oesophagus (Fyke *et al*, 1956; Atkinson *et al*, 1957). This high pressure zone has many of the characteristics of a physiological sphincter, but its precise importance in the regulation of gastrooesophageal competence has not been defined. It seems likely that the sphincter

FIG. 6. The effect of atropine on acid perfusion of the sphincter.

alone is not the only barrier to reflux but that it acts within an intricate mechanism in which local anatomical features and physiological activities are integrated as a functional unit.

In the present study the effect of a locally applied stimulus has been examined by exposing the gastric aspect of the sphincter to contact with hydrochloric acid in an effort to simulate a naturally occurring physiological stress. Surprisingly there have been few studies along these lines since Cannon (1908) showed in the cat that the activity of the cardia increased after the introduction of starch into the stomach, and postulated that the effect resulted from the stimulation of acid secretion. He further showed that the pressures required to open the cardiac sphincter when tested from the gastric aspect were greater when acidic solutions were used, a feature which persisted even after high bilateral cervical vagotomy. Robson and Welt (1959) repeated some of Cannon's experiments, and confirmed his findings. Clark and Vane (1961) also examined the gastrooesophageal sphincter in the cat and studied its nervous regulation. They showed an increase of rhythmic activity in the isolated sphincter in response to acid perfusion and demonstrated that the tone was markedly increased on changing from perfusion with N/100 to N/10 hydrochloric acid.

In man rhythmic movements at the cardia have not been demonstrated but it seems likely that the lower oesophageal sphincter exhibits tonic action, though the resting pressure may vary from day to day or to some extent between successive tests (MacLaurin, 1963). However, since perfusion with saline produced only minor changes in sphincteric pressure, the larger increases seen after perfusion with acid represent significant responses to this stimulus. Nevertheless consistent results were not

obtained, though the more acidic solutions were associated with the greatest increases in pressure. It may be significant that a solution at pH 3 was the most effective in this respect, for this is optimum for peptic activity in gastric juice.

The mechanism of the sphincteric response to acid is uncertain, but it seems probable that local receptors below the cardia are stimulated by contact with hydrochloric acid, and the increase in sphincter tone may be effected through a local myenteric reflex. The abolition of the response to acid after the injection of atropine supports this view and was not altogether unexpected, since Bettarello, Tuttle, and Grossman (1960) have demonstrated that anticholinergic drugs produce a sustained reduction in intraluminal sphincteric pressure.

It may be considered that the increased sphincteric pressures seen on perfusion with acid are unlikely to be sufficient to provide much of a barrier to reflux, particularly if there is a rise in intraabdominal pressure. However, with the sphincter in its normal intraabdominal position, increased intraabdominal pressure is distributed over the whole mechanism, and reflux results either when the sphincter is displaced, for example in hiatus hernia, or when intragastric pressure is greater than the pressure in and around the sphincter. The small pressure changes at the sphincter are likely to be compensatory for small changes in intragastric pressure such as may arise during a meal or on changing from the standing to the recumbent position. Further investigation

of patients with hiatus hernia using this technique may provide more insight into the problem.

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