Effects of oral magnesium sulphate on colonic motility in patients with the irritable bowel syndrome¹

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SUMMARY Magnesium sulphate, a substance known to cause release of cholecystokinin (CCK) from the small intestinal mucosa, was given by mouth (dose 0.1 g/kg in 150 ml water) to 20 patients with the irritable bowel syndrome. A rapid increase in colonic segmental motor activity (onset within two to six minutes in most cases) was seen (percentage activity increased from 16.2 to 23.7 $P < 0.05$; mean wave amplitude from 7.1 to 9.1 cm H_2O , NS; motility index from 144 to 259, $P < 0.01$). This increase was most marked in 10 patients who complained of attacks of abdominal pain after food (16.1 to 29.8%, $P < 0.01$; 6.8 to 9.6 cm H_2O , $P < 0.05$; 135 to 350, $P < 0.05$), and after the magnesium sulphate three of these patients experienced an attack of their usual pain. These findings provide further evidence that 'functional' abdominal pain after food may in some cases be related to an exaggerated intestinal motor response to cholecystokinin.

In approximately 40-50% of patients with recurrent abdominal pain for which no cause can be found ('functional' abdominal pain) the pain is precipitated or made worse by eating (Chaudhary and Truelove, 1962). Connell, Jones, and Rowlands (1965) demonstrated that in such patients colonic motility was often abnormal, with pronounced increases in intracolonic pressure after food. Holdstock, Misiewicz, and Waller (1969) confirmed the finding of abnormally increased colonic motor activity in patients with unexplained abdominal pain, and showed in some cases that the small intestine was similarly affected. The mechanism of this food-related hypermotility and pain has not yet been fully elucidated, but it seems possible that it could be mediated by one of the gastrointestinal hormones, several of which have motor effects on the gastrointestinal tract. Gastrin apparently has little effect on colonic motility (Misiewicz, Waller, and Holdstock, 1969), but fairly marked increases in the motor activity of the colon in normal subjects have been observed after intravenous cholecystokinin (Grossi, Messina, Del Duca, Ricci, and Messina, 1966; Dinoso, Meshkinpour, and Lorber, 1972). Similar changes were found in patients with the irritable bowel syndrome (Harvey and Read, 1973), particularly those with food-

related pain of the type described by Connell *et al* (1965), and four of eight such patients developed a typical attack of their usual pain after cholecystokinin, at the same time as markedly increased colonic motor activity was seen. In an attempt to ascertain whether endogenous CCK has a similar action, we have examined the effect on colonic motility of oral magnesium sulphate ($MgSO_4$), a substance which is a powerful stimulus to endogenous cholecystokinin release (Lyon, 1919; Boyden and Birch, 1930; Boyden, Bergh, and Layne, 1943; Harvey, Dowsett, Hartog, and Read, 1973).

Patients and Methods

Twenty patients with abdominal pain believed to be due to the irritable bowel syndrome were studied after an overnight fast. All were attending a gastroenterology clinic for investigation of abdominal pain, and routine examination and investigations (including sigmoidoscopy, barium studies and blood examinations) had failed to show a cause for their symptoms. Ten patients had food-related pain, and in the other 10 there was no relationship of the pain with eating.

Pressure changes within the sigmoid colon were recorded, as previously described (Harvey and Read, 1973), on a Devices M19 recorder, using miniature 7×10 mm balloons (Atkinson, Edwards, Honour, and Rowlands, 1957) placed 20-25 cm from the anus

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through a sigmoidoscope. After the balloons had been placed in position and the sigmoidoscope removed, the patients rested quietly on the couch for at least 60 minutes. They were then given 150 ml of water to drink and 30 minutes later were given magnesium sulphate (0.1 g/kg in 150 ml water) motility being recorded for a further 30 minutes. Motor activity in the 30 minutes after water and after magnesium sulphate was compared with that in the last 30 minutes of the initial fasting period by measuring the percentage duration of pressure waves, their mean amplitude, and a motility index (multiple of the other two indices). Probabilities were calculated by using Student's *t* test.

Results

No significant change in colonic motor activity was seen after water (percentage activity 16.2 to 14.2; mean amplitude of pressure waves 7.1 to 8.3 cm H₂O, motility index 144 to 133), but all parameters measured showed an increase after MgSO₄ (see table). The increase was most marked in the 10 patients whose pain was usually precipitated by eating (fig 1).

There was, however, a moderate overlap between the two groups, five of the 10 patients with pain unrelated to food showing increased motility after MgSO₄ and two of the group with food-related pain showing no increase. The high value for motility index after MgSO₄ in patients with food-related pain was not due merely to the inclusion of one or two particularly high values: even excluding the two highest, the mean value (209) was still greater than that for the patients with pain unrelated to food. Neither was the distribution of motility index in this group particularly skewed, five having values above and five below the mean.

The period of increased colonic motility usually began within a very short time of taking the MgSO₄ (2-14 minutes in 12 subjects, mean 4.9 minutes), with a fairly abrupt onset of activity, which increased

Fig 1 Changes in colonic motility, as motility index (mean and SE), after water and after MgSO₄. Little change occurred after water. After MgSO₄ the increase in activity was much more marked in the 10 patients with pain after food than in those whose pain was unrelated to eating.

to a peak within a few minutes and in most cases gradually subsided over the course of 20 to 30 minutes (fig 2). In other patients the increase in activity was more marked and more prolonged (fig 3). Three subjects experienced what they described as a typical attack of their usual pain during this period. Others experienced symptoms such as gurgling, 'windy feelings', fullness, belching, and passage of flatus per rectum in the period after MgSO₄ was given. There was no detectable quantitative or qualitative difference in motility response between the three patients who experienced pain after MgSO₄ and the remainder. In general, motor activity of the rectum was not affected (fig 2).

	Percentage Activity		Mean Wave Amplitude (cm H ₂ O)		Motility Index	
	Fasting	After MgSO ₄	Fasting	After MgSO ₄	Fasting	After MgSO ₄
All patients (n = 20)	16.2 ±3.0	23.7 ^a ±4.1	7.1 ±1.1	9.1 ^a ±1.9	144 ±33	259 ^a ±65
Patients with pain not related to eating (n = 10)	16.3 ±4.1	17.6 ^a ±5.1	7.3 ±1.7	8.5 ^a ±3.2	153 ±41	168 ^a ±60
Patients with pain after eating (n = 10)	16.1 ±4.6	29.8 ^a ±6.1	6.8 ±1.4	9.6 ^a ±2.1	135 ±53	350 ^a ±112

Table Motor activity of the sigmoid colon before and after oral MgSO₄¹

¹All values = mean ± SEM

^aN.S.

^bP<0.05

^cP<0.01

Fig 2 Effect of oral MgSO_4 on motor activity of the sigmoid colon and rectum in a woman with unexplained pain after meals. MgSO_4 was given as indicated by the deflections on the upper line. The increase in sigmoid activity was accompanied by pain identical to that typically experienced by the patient after food.

Fig 3 Effect of oral MgSO_4 on motor activity of the sigmoid colon and rectosigmoid in a 43-year-old woman with food-related pain. The pressure waves are not transmitted to adjacent segments of bowel (waves in the rectosigmoid occur independently of those in the sigmoid) and are thus 'segmenting' rather than peristaltic. Sporadic fast-wave activity can also be seen.

Discussion

The reason for the increased intestinal motor response in some patients with the irritable bowel syndrome to a number of different stimuli, eg, prostigmin (Chaudhary and Truelove, 1961), meals (Connell *et al*, 1965) or cholecystokinin (Harvey and Read, 1973), is not known. It has been suggested (Painter, 1972) that the different clinical varieties of the syndrome may represent a spectrum of responses to a diet depleted of plant fibre, and that the disorders would be better described as the 'irritated' bowel syndrome. As with meals (Connell *et al*, 1965) and cholecystokinin (Harvey and Read, 1973), there was a wide range of responsiveness of the colon to oral MgSO_4 . The greatest increases in motor activity were seen in those patients who usually experienced pain after food, whereas in subjects whose symptoms were not related to eating the increase was insignificant. However there was a moderate overlap between the responses in these two groups—some patients with food-related pain showing no increase in motility, whereas some whose symptoms were unrelated to food nevertheless showed increased motility after MgSO_4 . It seems therefore that these patients do not fall into two clear-cut and distinct groups, but that they represent a spectrum of differing degrees of responsiveness to the stimulus.

Magnesium sulphate has previously been shown to cause an increase in colonic motor activity (Davidson, Sleisenger, Almy, and Levine, 1956), but it is difficult to be certain about its mechanism of action. It is a powerful stimulus for the release of cholecystokinin from small intestinal mucosa, as was originally shown indirectly by studies of gallbladder contraction (Lyon, 1919; Boyden and Birch, 1930; Boyden *et al*, 1943) and more recently confirmed by direct radioimmunoassay measurement of serum levels of cholecystokinin in normal subjects after oral MgSO_4 (Harvey *et al*, 1973; Harvey, Grayburn, Jennings, and Hartog, 1974). Injection of this hormone results in an increase in both small intestinal (Adlercreutz, Pettersson, Adlercreutz, Gribbe, and Wegelius, 1960; Dahlgren, 1966; Parker and Bene-ventano, 1970) and colonic (Grossi *et al*, 1966; Dinoso *et al*, 1972; Harvey and Read, 1973) motor activity. It has been suggested that the action of cholecystokinin on the colon may be due to the arrival of ileal contents rather than to a direct motor effect of the hormone on the large bowel (Waller, Carvalhinhos, Misiewicz, and Russell, 1973).

Studying nine normal male subjects, Boyden *et al* (1943) showed that gallbladder contraction began on average one to five minutes after intraduodenal instillation of MgSO_4 . Berry and Flower (1971)

detected cholecystokinin release into portal blood within one minute of stimulation of the intestinal mucosa by HCl. It is probable, therefore, that release of cholecystokinin after MgSO_4 is very rapid, and the very early onset of increased colonic motor activity after MgSO_4 (fig 2) is consistent with a direct action of this hormone on the colon. It might be possible to assess the importance of other factors such as the entry of ileal contents into the colon (Waller *et al*, 1973) in patients with a double-barrelled colostomy or similar operative diversion, but we have not as yet had the opportunity to study such patients.

Abdominal pain apparently identical to that usually experienced after a meal was reproduced in three of our patients by MgSO_4 . A similar reproduction of typical pain by intravenous cholecystokinin has been reported in other groups of patients with functional disturbances of gastrointestinal motility (Harvey and Read, 1973; Dahlgren, 1964; Valberg, Jabbari, Kerr, Curtis, Ramchand, and Prentice, 1971). The findings of the present study provide further evidence that the intestinal hypermotility and pain after food in some patients with the irritable bowel syndrome may be due to an exaggerated motor response to endogenous cholecystokinin.

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