Motor activity recorded in the unprepared colon of healthy humans

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Abstract

A manometric method was developed to study the motor activity in the unprepared human colon, and the results in eight healthy subjects were compared with those obtained in the same subjects after bowel cleansing with a non-absorbable solution containing polyethylene glycol 4000 (PEG). A tube assembly (4.5 m long, 12 lumen) was introduced through the nose and passed through the gastrointestinal tract. Two manometric recordings were performed one month apart, one without any preparation and the other after bowel cleansing with PEG. There was no obvious qualitative difference between the recordings performed in the uncleaned and PEG cleaned colon. Moreover, in the unprepared colon motility indices were close to those measured in the cleaned colon. The number of high amplitude propagated contractions (mean (SEM)) was, however, higher in the cleaned colon (8.6 (2.8) v 5.4 (1.8)/subject/9 h in the unprepared colon; $p < 0.04$). It is concluded that in healthy subjects taking a regular diet, motor activity is not different between the uncleaned and cleaned colon with PEG, except for the high amplitude propagated contractions, which occur more frequently in the cleaned colon.

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In most studies on humans during the past two decades, electromyographic and manometric methods have been used to record colonic motor activity. The placement of recording probes introduced through the anus with the aid of colonoscopy requires premedication, air insufflation, and prior preparation to ensure the vacuity of the colon. Enemas, cathartics or oral solutions containing polyethylene glycol 4000 (PEG) are usually used for this purpose. Besides the ethical problems in the study of healthy subjects,¹ the invasive procedures required for probe placement raise the question of whether such techniques can even be truly physiological. The degree of distension or fullness, or both, of the large intestine may modify the colonic response to eating.²⁻⁴ There is also evidence that the motor activity of the colon may be affected by the volume and composition of dietary residues,²⁻⁵⁻⁹ the physicochemical nature of the luminal contents,¹⁰⁻¹¹ and the metabolic activity of the colonic flora.¹² For example, bile acids induce

colonic motor activity,¹³ which may be prevented by microbial metabolism of primary bile acids. Infusion of volatile fatty acids into the large bowel of sheep and pigs as well as into isolated rat colon has been shown to depress colonic motor activity.¹⁴⁻¹⁶ In rats, longterm administration of antibiotics dramatically reduces intestinal microflora and faecal excretion of volatile fatty acids and progressively increases colonic motility.¹² In addition to volatile fatty acids, other factors affected by their production (luminal pH, microbial growth, mineral absorption) may also account for changes in colonic motility.

In this study, we developed a manometric method to study the motor activity in the unprepared human colon, and we compared the results to those obtained in the same healthy subjects after bowel cleansing with PEG.

Methods

Subjects

Studies were performed in eight healthy volunteers (four female, four male, aged 19-34 years) with no history of gastrointestinal symptoms or gastrointestinal surgery, and having received no medication during the past two months. They had a normal whole transit time of radio-opaque markers (<67 hours¹⁷), and regularly ingested a normal Western diet, which contained 10-20 g of dietary fibre per day (average amount assessed for one week). Written informed consent was obtained from each subject before participating in the study, which was approved by the local ethics committee.

Colonic intubation

A tube assembly, which consisted of a 4.5 m long 12 lumen polyvinyl system was introduced through the nose. The tube assembly had an outer diameter of 6 mm and each lumen had an inner diameter of 0.5 mm. The 10 proximal lumens of the tube were intended for manometric recordings. Their side openings were at 15, 25, 35, 45, 50, 55, 60, 65, 70, and 75 cm respectively from the tip of the tube, and could be fluoroscopically located by metallic fragments. The tip consisted of the two last lumens ending inside a latex balloon containing mercury that could be filled with or emptied of air to facilitate the progression of the tube. The balloon was filled with 10-20 ml air when the gastroduodenal junction was passed and with 40-60 ml air when the caecum was reached. The migration of the tube was monitored by

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Figure 1: Abdominal x ray showing the manometric probe in the colon. Arrows show the position of catheter openings.

fluoroscopic control until the balloon was expelled through the anus. Eight catheter openings were then fluoroscopically selected in such a way that at least two of them explored the ascending colon, two the transverse colon, one the descending colon, and one the sigmoid colon (Fig 1). To standardise intestinal contents, the subjects were given a controlled diet containing 13–15 g of dietary fibre per day during the time required to pass the tube (median: 48 hours, range 24 to 60). At the end of the manometric recordings, the position of the catheter openings was checked, and the tube was cut under the nose. It was then expelled through the anus.

Manometric recordings

Intraluminal pressures were recorded by eight external pressure transducers (Gould Instruments, Ballainvilliers, France) connected to the catheters, which were continuously perfused

with distilled water by means of a low compliance perfusion system (flow rate 0.15 ml/min; total volume of water perfused per experiment was roughly 650 ml). The output of the transducers was connected to an eight channel amplifier coupled to a recorder (Gould Instruments, Ballainvilliers, France). Occlusion of the catheter openings yields a pressure rise of more than 80 mm Hg/s.

Study design

In each subject, two manometric recordings were performed in a random order at an interval of one month. One of the recordings was performed without any bowel preparation, and the other 18–24 hours after the oral ingestion of 3–4 litres of a non-absorbable PEG solution (64 g/l PEG 4000, 25 mmol/l NaCl, 10 mmol/l KCl, 20 mmol/l NaHCO₃, 40 mmol/l Na₂SO₄, osmolality 280 mmol/kg). The preparation was given until clear liquid rectal evacuations were obtained. The two manometric recordings started between 9 and 11 am. After three hours of basal recording during fasting, a 1000 kcal meal (20% protein, 50% carbohydrate, and 30% lipid) previously used in our laboratory to stimulate colonic motility¹⁸ was given and recordings were continued for six hours. During recordings, the subjects remained recumbent and were allowed to read and listen to music, but not to sleep. They were instructed to report any abdominal sensation with special attention to discomfort, need to defecate, borborygmi, and flatus.

Data analysis

The tracings were analysed visually to identify the different colonic motor events.¹⁹ Special attention was focused on the identification of high amplitude propagated contractions (HAPCs). These motor events were easy to recognise, because of their amplitude, which was more than 60 mm Hg, and their propagation over most of the length of the colon.^{19 20} Their frequency, origin, amplitude, propagation velocity, and relation with abdominal sensations were analysed. A quantitative analysis of the tracings was also carried out by calculating a motility index. All the recordings were digitalised at 30 minute intervals and the area under the curve of the tracings was calculated using a computer. Only contractions with amplitudes higher than 10 mm Hg above the baseline were included in the motility index. To compare the two manometric recordings, six recording points (two in the ascending colon, two in the transverse colon, one in the descending colon, and one in the sigmoid colon) were carefully selected in each subject in such a way that the sites of recording were as close as possible from one experiment to the other.

Statistics

Results were expressed as mean (SEM). Comparisons of motility index were performed by a three way analysis of variance, followed by

Figure 2: Manometric recording from the unprepared colon in a healthy volunteer. Note the colonic motor response to the test meal.

Figure 3: Number of HAPCs per subject per nine hours. The frequency of HAPCs was higher in the cleansed colon than in the uncleaned colon ($p < 0.04$ by the Wilcoxon signed rank test).

the Newman-Keuls test. The Wilcoxon signed rank test was used to compare HAPCs from recordings performed in the cleansed and uncleaned colon. In all instances, a p value < 0.05 was considered to be statistically significant.

Results

Motor activity in the uncleaned colon

This was characterised by phases of quiescence alternating with phases of activity (Fig 2). In all subjects, the motor activity was irregular, without any identifiable temporal organisation and was mainly represented by low amplitude contractions. Contractions were sometimes sporadic but most of them occurred in bursts lasting from 1 to 30 minutes at 3–6 cycles/min.

Overall, HAPCs were infrequent motor events. The mean number of HAPCs/subject per nine hours was 5.4 (1.8) (range: 0 to 18; Fig 3). All HAPCs originated in the caecoascending colon and 97% of them reached the sigmoid colon. Their mean amplitude was 104 (5) mm Hg, and was lower in the proximal colon (from the caecum to the splenic flexure) than in the distal colon (80 (8) *v* 120 (14) mm Hg; $p < 0.05$). The mean propagation velocity of HAPCs was 0.8 (0.1) cm/sec, and was lower in the proximal than in the distal colon (0.6 (0.1) *v* 2.0 (0.8) cm/sec; $p < 0.001$). Sixty per cent of HAPCs were felt by the subjects, mainly as a slight sensation of abdominal discomfort, or as a desire to defecate. Less frequently, they were associated with borborygmi or rectal passage of gas. Fifty one per cent of the HAPCs occurred in bursts, consisting of two or three successive contractions within 10 minutes; this pattern was more frequently associated with a desire to defecate (Fig 4).

Motor activity in the sigmoid colon was significantly higher ($p < 0.01$) than in the five other proximal recording sites (Fig 5) and

Figure 4: Grouped high amplitude propagated contractions recorded from the unprepared colon in a healthy volunteer. This pattern was associated with a desire to defecate.

Figure 5: Motility index per nine hours (mean (SEM)) in different parts of the PEG cleansed and uncleaned colon.

consisted mainly of prolonged low amplitude contractile waves. After ingestion of the meal, an increase in motor activity occurred within the 10 minute period after the beginning of the meal in the five proximal recording sites ($p < 0.05$), but it was not significant in the sigmoid area. This postprandial response was of short duration, the motility index being significantly higher only during the first 30 minutes after the meal, and consisted mainly of non-propagated contractions occurring in bursts (Fig 2).

Motor activity in the cleansed colon with PEG

There was no obvious qualitative difference between the recordings performed in the uncleaned and PEG cleansed colon. In the colon cleansed with PEG, however, the number of HAPCs was higher (8.6 (2.8) *v* 5.4 (1.8)/subject per nine hours; $p < 0.04$; Fig 3). The mean amplitude of HAPCs was similar in the cleansed and uncleaned colon (88 (4) *v* 104 (5) mm Hg) as well as their propagation velocity (1.0 (0.1) *v* 0.8 (0.1) cm/sec). As in the uncleaned colon, the propagation velocity of HAPCs was lower in the proximal colon than in the distal colon (0.7 (0.1) *v* 2.7 (0.3) cm/sec, $p < 0.001$). In the cleansed colon, 98% of HAPCs originated in the caecoascending colon, and 90% of them reached the sigmoid colon, a figure that was similar to the uncleaned colon. Forty three per cent of HAPCs moving in the cleansed colon were felt by the subjects. They occurred more frequently singly (70%) than in bursts.

At the six recording sites, the motility indices in the cleansed colon were not significantly different to those measured in the uncleaned colon (Fig 5). As in the uncleaned colon, the motility index in the five proximal recording sites increased significantly for the first 30 minutes after the meal ($p < 0.05$). The motility index in the cleansed sigmoid colon was significantly higher than in the other recording sites ($p < 0.05$) and did not change significantly after eating (Fig 5).

Discussion

An important problem in recording colonic motor activity in humans is that the colon has to be emptied to position a recording device by colonoscopy. The consequences of such a

manoeuvre on motor activity of the human colon have not been assessed, except for the rectosigmoid portion.²¹ Our data show that there is no prominent difference in the pattern of motor activity between the cleansed and uncleansed colon. Our results in the unprepared colon are in agreement with those previously obtained by manometry in an empty colon.^{19,20} Indeed, in both the uncleansed and PEG cleansed colon, motor activity was characterised by irregular occurrence of phases of quiescence, alternating with non-propagated contractions occurring singly or in bursts, and HAPCs. The motor activity was higher in the sigmoid colon, and increased after eating in the other segments of the colon. More than half of HAPCs were felt by the subjects. This high correlation between HAPCs and subjective feelings may result from the unusual situation in which abdominal sensations were readily and carefully recorded by the healthy volunteers. It cannot be excluded that some abdominal sensations arise from the traction effect of HAPCs on the manometric tube itself providing a sensory stimulus to another regions of the gastrointestinal tract. Recording the normal colon by retrograde insertion of a manometric probe, Narducci *et al*¹⁹ found, however, a similar high level of concordance between HAPCs and subjective feelings.

In the colon cleansed with PEG, the mean motility indices from the six colonic sites were close to those measured in the uncleansed colon. Compared with the uncleansed colon, the motility indices in the cleansed colon were higher in five of eight subjects, and were lower in the remainder. Similar results could therefore be anticipated if a higher number of subjects had been studied. Dinoso *et al*²¹ compared the rectosigmoid motor activity in humans with or without prior bowel cleansing. These authors found that cleansing did not affect significantly the motility index in the rectosigmoid colon. As perfused catheters are said to record only contractions that are strong enough to occlude the lumen around the openings of the catheters, it could be supposed that the degree of occlusion related to colonic contractions may be less in the absence of the colonic contents. Nevertheless, simultaneous recording of colonic motor activity in dogs with serosal strain gauges and open tipped tubes has shown good agreement of both shape and amplitude of colonic contractions.²² In our study, the amplitude of HAPCs and the motility index from the sigmoid colon were slightly lower in the cleansed colon, but an opposite variation was found with regard to the motility indices in the five proximal sites of recording. Thus, we do not believe that changes in the sensitivity of the recording technique may account for the lack of differences between the uncleansed and cleansed colon.

In the colon cleansed with PEG, we found that the mean number of HAPCs increased by 60%. The low perfusion rate used in our study does not affect motility in the unprepared colon.^{23,24} At this rate, 650 ml of water were delivered throughout the colon over the nine hours of the study, a volume within the

absorption capacity of the healthy colon.²⁵ In the empty unaccommodated colon, however, we cannot rule out that this extra fluid might have a stimulating effect and play a part in the increased number of HAPCs. In a study, Sarna²⁶ investigated the effect of cleansing on colonic motor activity in dogs with serosal strain gauge transducers. He found that 18–20 hours after cleansing the colon with fluids (absorbable electrolyte or Colyte solution), the frequency of giant migrating contractions was higher than in the uncleansed colon. The higher number of HAPCs we found in the empty human colon might thus be attributed to the stimulating effect of colonic lavage with PEG performed on the previous day. The frequency of HAPCs has been found to be increased in diarrhoeas induced by cathartics,^{27,28} or occurring in ulcerative and experimental colitis.^{29,30}

Our study provides further insight into colonic motility in humans, in particular the prominent pattern HAPCs. In both the uncleansed and PEG cleansed colon, most of HAPCs started in the ascending colon and migrated caudally over the entire colon, with an increased velocity from the proximal to the distal colon. The mean frequency of HAPCs recorded by perfused catheter systems in the empty colon varied from 4.4–6.9/24 hours in earlier studies^{19,31} to one per hour in a more recent report using a computer program.³² The frequency of migrating long spike bursts, which are thought to be the myoelectrical equivalent of HAPCs, also averaged one per hour.³³ Using three tube mounted strain gauges spaced 45 cm apart, HAPCs were, however, reported by Soffer *et al*³⁴ to occur very infrequently (no more than 2/24 hours) in a normal unprepared colon. The reasons why we found a high frequency of HAPCs might be the better recognition of this motor pattern, resulting from the constant access to the ascending colon where HAPCs started, and the greater number of closely spaced recording sites. The number of HAPCs has been shown to vary greatly between subjects^{20,32} and these individual variations can also explain why we recorded a higher number of HAPCs, especially in one of the healthy volunteers (Fig 3). Amplitude of HAPCs was significantly lower in the proximal than distal colon, but this could simply be caused by the larger diameter of the proximal colon, which can attenuate pressure variations over recording sites. Propagation velocity of HAPCs was also faster in the distal than in the proximal colon; it is possible that differential sleeving of the colon over the manometric tube might contribute to this difference.

Our manometric technique, which obviates the need for colonic cleansing, does not change the metabolism of colonic flora, nor remove the colonic contents, which can offer a resistance to motor activity and propulsion. It allows regular access to the proximal colon, which is difficult to study with retrograde intubation. Colonic motor activity in response to the infusion of nutrients or drugs into the ascending colon can also be recorded, without the risk

of expelling the probe through the anus.³⁵ The method avoids the problem of colonoscopy in healthy volunteers, is well tolerated, but has some limitations. Firstly, it takes 24–60 hours for the tube to pass through the gut, a time that could be shortened by using a two stage per nasal technique to position the tube in the colon, as proposed by Soffer *et al.*³⁴ Secondly, the subjects are not ambulatory, a condition that can reduce colonic motility.³⁶ Thirdly, the method probably does not work in patients who have severe motor disorders because of decrease in the motility needed to propel the tube. Lastly, as with other colonic intubation techniques, it cannot be ruled out that the manometric tube may induce motor changes.

In conclusion, despite the lack of semi-solid contents in the colon cleansed with PEG, the fundamental colonic motor profile does not seem noticeably different to that recorded in the unprepared colon. This finding reinforces a posteriori the physiological validity of previous manometric studies performed by retrograde insertion of recording probes in the cleansed colon. We studied, however, healthy volunteers taking a regular diet. Our data do not rule out that differences may appear between the emptied and normal colon, when in the normal colon the contents are modified by dietary supplements with unavailable carbohydrate or by increased delivery of unabsorbed nutrients from the small intestine. In the colon cleansed with PEG, HAPCs occurred more frequently. As these motor events play an important part in colonic transit,^{29–37} our manometric technique may represent a suitable method to study concomitantly the relations between the motor activity and propulsion assessed by isotopic techniques in the human colon.

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