Gut 1995; **37**: 270–273

Acute diarrhoea induces rectal sensitivity in women but not men

L A Houghton, J Wych, P J Whorwell

Abstract

Some patients with diarrhoea predominant irritable bowel syndrome have increased rectal sensitivity. It is uncertain, however, whether the diarrhoea is a consequence of the rectal sensitivity or if it is sensitising the rectum in some way. The aim of this study was to assess whether inducing diarrhoea in normal healthy volunteers can sensitise the rectum and therefore be a potential or partial cause of the sensitive rectum seen in some patients with diarrhoea predominant irritable bowel syndrome. The anorectal responses to balloon distension were measured in 20 healthy volunteers (aged 20–43 years, 10 female) eight hours after laxative induced diarrhoea or under control conditions. Ingestion of an iso-osmotic laxative increased stool output from 1·1 (0·7–2·3) (median (range)) to 8 (5–19) bowel movements per day with no significant differences between men and women. In women rectal sensitivity was significantly increased after diarrhoea compared with control conditions (vol to induce discomfort (ml): 116 (96, 136) *v* 153 (137, 168), mean (95% CI); $p<0·001$). This was associated with a reduction in the volume to induce internal anal sphincter relaxation (16 (12, 20) *v* 28 (21, 36); $p<0·005$), and volume to induce sustained internal anal sphincter relaxation (70 (56, 84) *v* 90 (67, 113); $p<0·03$), but no significant change in rectal compliance (ml/cm H_2O at 100 ml) 4·8 (3·5, 6·1) *v* 4·1 (3·0, 5·1) or distension induced motility (motility index) 994 (341, 1647) *v* 735 (46, 1424). Conversely, in men diarrhoea had no significant effect on anorectal physiology and their control values were not significantly different from those of the women. In conclusion, the results of this study taken with the finding that irritable bowel syndrome is more common in women, suggests that the male or female sex hormonal environment may be an important factor in allowing the gut to be sensitised to noxious stimuli.

(*Gut* 1995; **37**: 270–273)

Keywords: diarrhoea, anorectal physiology.

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Accepted for publication 31 December 1994

Irritable bowel syndrome patients who present with diarrhoea often have abnormally enhanced rectal sensitivity, as reflected by reduced thresholds for the perception of wind, the desire to defecate, and pain when the rectum is distended.[1 2] These patients also have abnormally reduced rectal compliance and they generate rectal contractions and internal anal sphincter relaxations at abnormally low volumes of rectal distension.[2]

It is not known, however, whether it is the presence of diarrhoea that is inducing these changes in anorectal sensitivity and contractility or whether the diarrhoea is a consequence of the increased motility/sensitivity.

The aim of this study was therefore to assess whether inducing acute diarrhoea in normal healthy volunteers leads to increases in rectal sensitivity and contractility.

Methods

Subjects

Twenty normal healthy volunteers (aged 20–43 years; 10 male) participated in the study. No subject experienced any chronic gastrointestinal symptoms nor had a history of anxiety disorders or other psychiatric illness. All subjects completed the Hospital Anxiety and Depression questionnaire, which allows a score to be calculated to detect the presence of abnormal anxiety or depression. None of the subjects were receiving regular medical treatment, other than three of the female volunteers who were taking oral contraceptives. All subjects gave written informed consent and the study was approved by the local ethical committee.

Protocol

Each subject was studied on two occasions, separated by at least two weeks; once after acute diarrhoea induced with an osmotic laxative, and once under controlled conditions. The osmotic laxative used was Klean-Prep (consisting of 236 g polyethylene glycol 3350, 22·7 g sodium sulphate, 6·74 g sodium bicarbonate, 5·86 g sodium chloride, and 2·97 g potassium chloride/4 litres; licensed under Birex Pharmaceuticals, Republic of Ireland, distributed by Norgine Ltd, Oxford), which when reconstituted in four litres of water provides an iso-osmotic solution for cleansing the bowel. In this study, however, we only used half of the recommended dose (two litres) and flavoured the solution with orange juice to improve palatability. The control solution was two litres of orange juice. Both solutions were drunk within one hour and the order of the studies was randomised.

Eight hours after ingestion of the laxative, a multilumen polyvinyl catheter (Arndorfer Medical Specialties, Wisconsin, USA) was inserted into the rectum and positioned with

TABLE I *Effect of administration of the osmotic laxative on bowel frequency*

	Control (day^{-1})	*Diarrhoea (day^{-1})*
Men (n=10)	1·4 (1·0–2·3)	7·5 (5·0–19·0)*
Women (n=10)	1·1 (0·7–1·4)	10·0 (5·0–12·0)*

Results expressed as median and range.
*Statistically significantly different from control ($p<0·0001$).

two side holes in the rectum (4·5 and 15·0 cm from the anal verge) and three side holes in the anal sphincter (0·5, 1·0, and 2·0 cm from the anal verge). Each side hole was perfused with water at a rate of 0·2 ml/min^{-1} (Arndofer Medical Specialities) and connected by water filled transducers to a polygraph recorder and visual display unit (Synectics Medical, Sweden). A 6 cm length of distensible latex tubing was tied to the catheter between 5 and 11 cm from the anal verge and used to distend the rectum. The pressure within the rectal balloon was monitored using a water filled non-perfused channel sited at 8 cm from the anal verge.

After a 10 minute basal recording period, the rectal balloon was serially inflated with air at 10, 20, 40, 60, 80, 100 ml, and then in 25 ml increments until the subject experienced discomfort. Inflations were maintained for one minute, and were separated by periods of at least 30 second in which the balloon was totally deflated. During the procedure the subjects were asked to mark on a standard pro forma the nature of any sensation felt ('sensation', 'wind', 'open bowels', 'urgency', and 'discomfort'). Although the subjects were informed at the beginning of the study of the nature of the sensations they might expect to feel, they were not aware of the timing of balloon distensions or prompted about the sensations during the studies.

Analysis of data

The following measurements were derived from the anorectal study: (i) The lowest balloon volumes required for initial perception and to induce the sensations of gas, call to stool, urgency, and discomfort. (ii) The steady state pressure in the rectal balloon at each distending volume and the rectal compliance (calculated from the volume:pressure relation at 100 ml distension). (iii) The lowest balloon volume required to induce repetitive rectal contractions, defined as a sequence of more than four consecutive contractions.[3] (iv) The rectal motility index during distension calculated by summing the area under the rectal pressure profiles at 4·5 and 15 cm from the anal verge. (v) The basal anal pressure. (vi) The lowest distending volume required to initiate internal anal sphincter relaxation and to cause relaxation sustained throughout the distension.

TABLE II *Effect of laxative induced diarrhoea on rectal sensation*

	Control (ml)	*Diarrhoea (ml)*
Perception		
Men	20·0 (–, –)	17·5 (12·2, 22·8)
Women	12·5 (10·0, 15·0)	12·5 (10·0, 15·0)
Gas		
Men	34·4 (25·8, 43·1)	40·0 (26·7, 53·3)
Women	28·8 (18·2, 39·3)	17·5 (8·7, 26·3)*
Stool		
Men	60·0 (43·2, 76·8)	66·0 (50·6, 81·4)
Women	60·0 (49·2, 70·8)	38·9 (22·4, 55·4)*
Urgency		
Men	103·0 (73·2, 132·9)	105·5 (77·8, 133·2)
Women	109·0 (89·9, 128·1)	78·0 (63·5, 92·5)*
Discomfort		
Men	145·5 (100·8, 190·3)	153·0 (94·3, 211·7)
Women	152·5 (136·6, 168·4)	116·0 (96·4, 135·6)*

Results expressed as mean and 95% CI.
*Statistically significantly different from control $p<0·025$.

Statistical analysis

Wilcoxon signed rank test was used to assess the significant differences between the parameters recorded under control and diarrhoea conditions.

Results

Bowel habit

Between two and three hours after ingestion of the iso-osmotic laxative all volunteers experienced an increase in bowel frequency increasing from 1·1 bowel movements per day (0·7–2·3 day^{-1}) (median (range)) to 8·0 bowel movements per day (5·0–19·0 day^{-1}) ($p<0·0001$). There was no significant differences in bowel habit between the male and females volunteers under both control and diarrhoea conditions (Table I).

Anorectal parameters

Inducing acute diarrhoea in the female but not the male volunteers, significantly increased rectal sensitivity to balloon distension, in that the volume required to induce the sensation of gas, call to stool, urgency, and discomfort were significantly lower than under control conditions ($p<0·025$) (Table II).

Although the volumes required, however, to induce the initial and sustained internal anal sphincter relaxations were also significantly reduced under diarrhoea conditions compared with control conditions for the female ($p<0·025$) but not male volunteers, inducing diarrhoea did not significantly change rectal compliance, the volume to induce repetitive rectal contractions, motility index, or the basal anal sphincter pressure for both the male and female volunteers (Table III).

Psychopathology

None of the volunteers scored positively for anxiety or depression on the Hospital Anxiety and Depression questionnaire, and there were no significant differences in anxiety scores between the male (5·0 (3·6, 6·4); mean (95% CI)) and female (5·4 (3·3, 7·5)) volunteers, nor in depression scores between the male (1·0 (0·1, 2·0)) and female (1·1 (0·3, 1·9)) volunteers.

Sex hormone status of female volunteers

There seemed to be no association between the degree to which the anorectum responded to

TABLE III *Effect of laxative induced diarrhoea on anorectal motility*

	Control	Diarrhoea
Rectal compliance (ml/cm H_2O at 100 ml)		
Men	4·7 (2·7, 6·8)	4·3 (3·0, 5·6)
Women	4·1 (3·0, 5·1)	4·8 (3·5, 6·1)
Rectal motility		
Vol for repetitive contraction (ml)		
Men	81·2 (−17·1, 179·5)	88·8 (2·1, 175·5)
Women	66·7 (48·2, 85·2)	80·0 (47·8, 112·2)
Motility index		
Men	779 (202, 1357)	473 (215, 731)
Women	735 (46, 1424)	994 (341, 1647)
Anal parameters		
Basal pressure (cm H_2O)		
Men	88·8 (75·5, 102·1)	92·2 (79·0, 105·5)
Women	90·5 (75·6, 105·4)	84·9 (70·0, 99·7)
Vol to induce IAS relaxation (ml)		
Men	32·0 (18·4, 45·6)	39·0 (20·1, 40·9)
Women	28·0 (20·5, 35·5)	16·0 (12·2, 19·8)*
Vol for sustained IAS relaxation (ml)		
Men	88·0 (62·4, 113·6)	81·5 (55·7, 107·3)
Women	90·0 (67·4, 112·6)	70·0 (55·9, 84·1)*

Results expressed as mean (95% CI).
*Statistically significantly different from control $p<0·025$.
IAS=internal anal sphincter.

the diarrhoea and the menstrual or contraceptive status of the female volunteers.

Discussion

This study has shown that acute diarrhoea induced with an iso-osmotic laxative significantly increases the sensitivity of the rectum to balloon distension and reduces the distension volume required to induce the initial and sustained internal anal sphincter relaxations in female but not male volunteers. Rectal compliance, distension induced contractility, and the motility index, however, were unaffected by diarrhoea in both the female and male volunteers.

The changes to rectal sensitivity and anal sphincter activity induced by diarrhoea in the female volunteers could show that at least in part the abnormal anorectal motility and sensitivity seen in irritable bowel syndrome patients is secondary to their diarrhoea; although the specific mechanisms of sensitisation could be different in the two groups. The fact that the anorectal physiology of the male volunteers was not affected does not necessary contradict this possibility, as there are data to suggest that women have a reduced visceral sensitivity threshold to lumenal stimuli, such as rectal distension[4] and intestinal nutrients[5 6] compared with men. Exactly why women may have a lower visceral sensitivity threshold is unknown, but it is possible that it may be related to the sex steroid hormones, particularly as irritable bowel syndrome is more common in women, both in those seeking health care[7–10] and in those who do not.[11 12] Female sex hormones have been shown to influence oesophageal,[13] gastric,[14] small and large bowel[15 16] motility, as well as gall bladder motility.[17 18] A recent study conducted by ourselves showed, however, that the menstrual cycle does not affect anorectal motility or sensitivity.[19] In addition, in this study there seemed to be no association between the degree to which the anorectum responded to the diarrhoea and the menstrual or contraceptive status of the female volunteers, suggesting that the presence of female sex hormones rather than their cyclical changes are more important. Furthermore, the role of male sex hormones possibly preventing sensitisation in some way is worthy of further consideration. Anxiety has also been implicated in increasing visceral sensitivity,[2 20] but did not seem to be a significant factor in our study as there were no significant differences in either the anxiety or depression scores between the female and male volunteers.

The finding that there was no concomitant reduction in rectal compliance or increase in distension induced phasic activity in the female volunteers, as reported to occur in irritable bowel syndrome patients with rectal sensitisation,[2] could be explained if the changes in motility are secondary to rectal sensitisation. Thus it might be expected that an eight hour acute period of diarrhoea, compared with chronic diarrhoea in irritable bowel syndrome patients, may not be long enough to change rectal contractility. Evidence for this comes from the fact that rectal compliance can be reduced in normal subjects by increasing the rate of ramp distension, but sensitivity is not enhanced under these circumstances, it is reduced.[21]

In conclusion, our data suggest that diarrhoea can sensitise the rectum, and may at least in part be responsible or potentiate the sensitivity of the rectum of irritable bowel syndrome patients. It also emphasises the point that physiological studies on the lower gut for research purposes should always be performed on the unprepared bowel.

This work has been published as an abstract in *Gut* 1993; **34** (suppl 4): S3. We thank Julie Morris, Senior Statistician, for her help in the statistical analysis.

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