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Colonic Motor Function in Humans Is Not Affected by Gender

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Functional abdominal pain, including the irritable bowel syndrome, is more common in females. Our aim was to determine if differences in motility or biomechanical properties of the colon could account for this gender difference. In 18 healthy subjects (nine males), a catheter assembly incorporating a balloon and perfused side holes, connected to a barostat, was positioned in the left colon. The system was used to determine compliance, sensation in response to phasic balloon distension, and changes in motor activity and tone in response to a meal. There was no significant difference in any of these variables between males and females. We conclude that there is no gender difference in colonic motor function or sensation to balloon distension. The increased prevalence of irritable bowel syndrome in females may be related to psychosocial factors rather than differences in colonic motor function.

KEY WORDS: colon; motility; gender; tone; perception; barostat.

Functional gastrointestinal disorders are common in the general population (1). A number of studies have shown that these disorders, in particular irritable bowel syndrome (IBS), are more prevalent in females than in males (2–6). The pathophysiology of these disorders remains unclear, with recent research focusing on altered visceral perception as one of the mechanisms. Because female hormones can affect smooth muscle function, they may change the biomechanical properties of the gut wall and, as a result, affect visceral perception. The aim of this study was to determine if variables of colonic motility and tone, as well as colonic perception to balloon distension differ between males and females.

MATERIALS AND METHODS

Subjects. Eighteen healthy subjects, nine males (mean age 47.7 years ± 2.4) and nine females (mean age 56 years ± 2.6) were recruited from our flexible sigmoidoscopy screening clinic. They had no history of medical problems or use of medications that could affect gut motor function. None had any abdominal operation (except for cholecystectomy, appendectomy, and hysterectomy). Sigmoidoscopy was done for screening purposes only in all subjects. All participants signed informed consent for the study, which was approved by the Institutional Review Board at the Cleveland Clinic.

Equipment. Colonic motor function was evaluated by a multilumen catheter, incorporating a polyethylene barostat balloon and perfused lumens. An infinitely compliant balloon, 10 cm long with a maximal volume of 1000 ml (Zynetics) was connected to a barostat (Medtronic) for colonic distension and measurement of colonic tone. Four water-perfused channels were incorporated for pressure measurement and side holes were positioned 5 and 10 cm proximal and distal to the balloon. Each lumen was perfused at a rate of 0.4 ml/min, and pressure was recorded by volume displacement transducers connected to the perfusion pump. The balloon and perfused ports were positioned under fluoroscopy in the descending colon with the aid of a colonoscope.

Colonic Compliance. Compliance was determined by changes in balloon volume in response to 4 mm Hg increments in intraballoon pressure up to 40 mm Hg. Each distension was maintained for 1 min, with a 1-min deflation period in between. Two compliance sequences were performed, with an interval of 5 min between the two, and the

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second sequence was used for analysis of compliance curves (7).

Colonic Response to Food. Changes in colonic tone, number of contractions, and motility index were measured for 20 min before and 45 min after eating a standard meal including a hamburger, mashed potatoes, milk, and cookies which provided a total of 800 kcal (44% fat, 36% carbohydrates and 20% protein). Balloon pressure was set at 2 mm Hg above the lowest pressure at which respiratory excursions could be seen and was defined as the operating pressure (8). The median value was 14 mm Hg (in six subjects respiratory oscillations could not be clearly determined and the operating pressure was set arbitrarily at 14 mm Hg).

Colonic Sensation. Sensation of gas, urge to defecate, or pain was assessed in response to intermittent, random increases in intraballoon pressure to levels of 8, 16, 24, and 32 mm Hg above the operating pressure (8). Each distension was maintained for 1 min with 1 to 2-min intervals when the balloon was deflated. Sensations were rated at 20 sec after distension by marking a line on a 100-mm-long visual analog scale, with descriptors of "unnoticeable" and "unbearable" at each end. For analysis, balloon volume was evaluated for a period of 40 sec following inflation.

Experimental Design. Studies were done after an overnight fast. Following two enemas (Fleets), a colonoscope was passed to the transverse colon, and a guidewire was introduced. The colonoscope was then removed, while deflating the colon. The catheter was advanced to the descending colon over the guidewire, under fluoroscopic guidance. Each subject was sedated with midazolam (2 mg intravenously) prior to the procedure, followed by reversal of sedation with flumazenil (0.2 mg intravenously) after catheter placement. After an equilibration period of 60 min, the study protocol started. Compliance curves were obtained first, followed by assessment of sensation, which was obtained again 45 min after the meal.

Compliance. The pressure–volume relationship was analyzed by averaging the balloon volume over the 60 sec of inflation. We used a power exponential model, as described by Bharucha et al (8), to fit the nonlinear compliance curve, with parameter β representing the overall shape of the curve, κ the change in balloon volume as a function of 1/pressure at any given point, and $P½$ the pressure at which half-maximum barostat volume is reached.

Colonic Motility. The frequency of contractions and motility index were calculated by a dedicated software (Medronic). Contractions with an amplitude >10 mm Hg above baseline, duration of 1.5–60 sec, and an interpeak interval >1.5 sec were selected for analysis (8).

Statistics. Paired and unpaired *t* tests were used for comparison of motility data and tone within and between the gender groups. For analysis of sensation scores over the range of distending pressures, we used a mixed model analysis of variance with barostat volume and gender as effect variables and period (fasting or postprandial) as a covariate. Wilcoxon rank-sum test was used for analysis of compliance variables. Data are presented as median or mean ± SEM; $P < 0.05$ for significance.

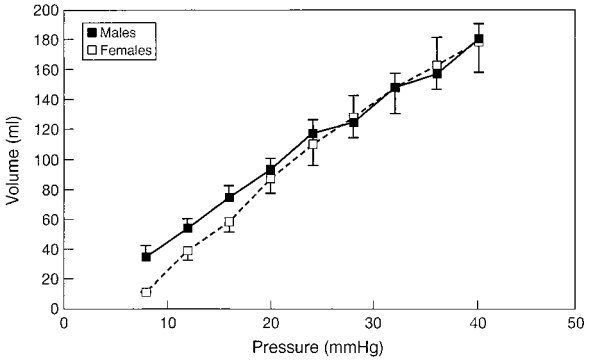

Fig 1. Pressure/volume relationship in males and females.

RESULTS

Compliance. Figure 1 shows the pressure–volume curves of the two groups, and the variables analyzed are presented in Table 1. Compliance was not significantly different between the groups.

Colonic Sensation. Figure 2 shows the VAS scores for the various perceptions in both groups during fasting. There was no difference between the groups. There was also no difference in perception between the groups in the postprandial state, or within groups between both states (not shown).

Colonic Motility. Number of contractions, motility index, and balloon volumes before and after the meal are shown in Table 2. While motility indexes and tone (reflected by the reduced balloon volumes) were increased after a meal, they were not different between the two groups.

DISCUSSION

The pathophysiology of functional gastrointestinal disorders, including IBS, is still unclear. A number of mechanisms have been contemplated, such as abnormal motility, psychiatric disorders, and heightened visceral perception (9). The reasons for the increased prevalence of IBS among females (2–6) are not clear but could be related to differences in any of the mechanisms cited above.

TABLE 1. COMPARISON OF COMPLIANCE CURVES BETWEEN MALES AND FEMALES*

Parameter	*Females*	*Males*
Kappa	27.2 (25.1–31.2)	24.9 (22.2–32.9)
Beta	0.86 (0.74–1.0)	0.87 (0.78–1.23)
$P½$ (mm Hg)	18.8 (12.1–23.4)	14.7 (10.6–23.4)

*Values are presented as median with range (25th–75th percentiles) in parentheses.

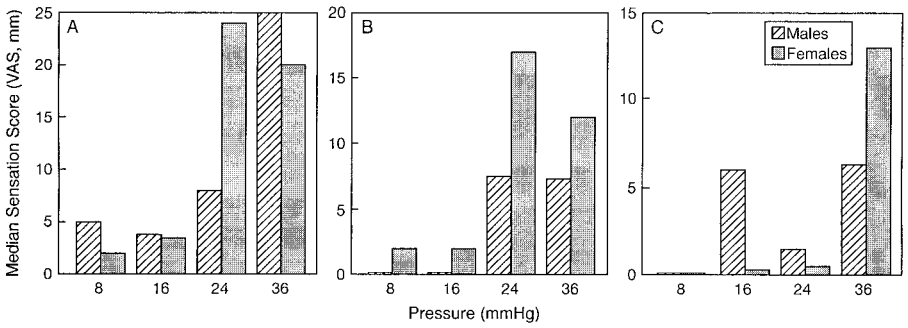

Fig 2. Median visual analog scores for gas (A), urge to defecate (B), and pain (C), in males and females, during fasting. There is no statistical difference between the groups.

One possible reason for the gender difference in the prevalence of IBS is the effect of female hormones on smooth muscle function. Progesterone is a smooth muscle relaxant, and so it is possible that the different hormonal milieu in the two phases of the menstrual cycle may affect bowel function and as a consequence perception. Alteration in compliance can affect perception since a given intraluminal volume is associated with different intraluminal pressures, resulting in different wall tensions. However, results of studies on the effect of the menstrual cycle on gut function are conflicting. Lower esophageal sphincter pressure was found to be reduced and gastrointestinal transit was found to be prolonged in the luteal phase in some studies (10, 11), while others showed no differences in these variables between the luteal and follicular phases (12, 13). Of interest, a study using esophageal balloon distension to induce esophageal pain found no difference in pain thresholds in women studied in both phases of the menstrual cycle (14). We have found no difference in the compliance of the left colon between our male and female subjects. We made no attempt to control for the phase of the menstrual cycle, but most of the women in the study were postmenopausal. Because mechanoreceptors in the gut wall are affected by wall tension (15), which depends on the diameter of the viscous, changes in the size of the gut can possibly affect pain perception. Although this study does not allow for accurate measurement of colonic diameter, it is unlikely to be different between the two groups. The cylindrical shape of the polyethylene barostat balloon, the overlapping compliance curves, and the results of the analysis of the pressure–volume relationship suggest that the diameter of the colon was comparable among males and females.

There were no differences in the other motility variables studied. The number of contractions and motility index during fasting and following food, as well as the changes in colonic tone induced by food, were comparable between males and females.

Perception of gas, urge to defecate, and pain in response to balloon distension was not different between the groups. Other groups have shown that in healthy subjects, females have a lower threshold to esophageal pain induced by balloon distension than males (14). The negative results of our study may be related to differences of technique, analysis of perception scores, or the different gut segment being studied. Because patients with functional gastrointestinal syndromes tend to be more symptomatic following meals, we also evaluated the effect of food on colonic sensations. There was no difference in sensation scores between the fasted and postprandial state in either group of subjects. This suggests that in healthy subjects the neural and hormonal changes induced by food do not enhance afferent mechanisms responsible for visceral sensation.

TABLE 2. VARIABLES OF COLONIC MOTILITY, BEFORE AND AFTER MEALS, IN MALES AND FEMALES*

	Fasting			*Postprandial*		
	Contractions/min	*MI*	*Vol (ml)*	*Contractions/min*	*MI*	*Vol (ml)*
M	0.71 ± 0.10*	6.46 ± 0.38†	72.5 ± 9.79	0.87 ± 0.11	9.68 ± 0.33	45.98 ± 9.90
F	0.52 ± 0.10	5.18 ± 0.80†	59.7 ± 13.84†	0.62 ± 0.22	8.11 ± 0.85	31.22 ± 8.22

*None of the variables was significantly different between the groups.
†$P < 0.05$ fasting compared to postprandial values.

The pathophysiology of IBS remains unclear. While abnormal motor function has been described in various segments of the gut in patients with IBS, the concept that this entity is caused by a primary motor abnormality is yet to be established (16). More recent research efforts have explored the possibility that heightened visceral perception may be a dominant mechanism in IBS (17, 18), with evidence of heightened perception to balloon distension of the colon (19) and small bowel (20) in patients with IBS. Psychological factors have been studied as well. Patients with IBS have been shown by some studies to be more likely to suffer from disturbances such as depression, anxiety, or somatization (21, 22). Patients with the syndrome who seek medical advice have a higher frequency of psychological disturbances than persons who do not seek medical help (23, 24). Sexual and physical abuse can contribute to increased referral rates in IBS patients and refractoriness to treatment (25, 26). Finally, a history of abuse is much more frequent in females, both in the community (27) and in clinical populations (28). Our study suggests that in healthy subjects, there is no difference in colonic motility or sensation between males and females. Perhaps psychological distress related to abuse contributes to the increased prevalence of IBS in female patients.

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