Clinical, Physiological, and Psychological Correlates of the Improvement of Defecation during Menses in Women with Functional Gastrointestinal Disorders

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Keywords

Pelvic pain · Irritable bowel syndrome · Functional bowel disorders · Depression · Anxiety · Colonic transit time · Anorectal manometry

Abstract

Background/Aims: Little is known about the improvement in defecation frequently reported by women around menses. We aimed to describe clinical, physiological, and psychological correlates of this improvement in those with functional bowel disorders. **Patients and Methods:** We recruited 478 consecutive premenopausal adult females with no indication of gynecologic or psychiatric disease, who were attending an outpatient functional bowel disorders clinic. Patients completed a Rome III questionnaire, psychological evaluation stool form, and a 10-point Likert scale for constipation, diarrhea, bloating, and abdominal pain. These patients underwent physiological tests, anorectal manometry, and colonic transit time and were classified according to the presence or the absence of improvement in defecation during menses. The reverse selection procedure was used for model selection during multivariate logistic regression where statistically significant variables ($p < 0.01$) remained in the adjusted model. **Results:** Ninety-seven patients (20%) reported easier defecation during menstruation. These pa-

tients were younger ($p < 0.001$) but had similar body mass indices and psychological profiles as the other patients. Clinically, they only reported more frequent irritable bowel syndrome (IBS) with constipation ($p = 0.007$), with harder stools ($p = 0.005$) and delayed left colon transit time ($p = 0.002$). No anorectal manometric parameter was different between the 2 groups. **Conclusion:** Improvement of constipation during menses is mainly associated with younger age and constipation-IBS phenotype and not with functional constipation.

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Introduction

The therapeutic relief of irritable bowel syndrome (IBS) symptoms following hysterectomy [1] and the experimental [2] and clinical [3] action of progesterone on chronic constipation suggest that the fluctuation of hormonal levels during the menstrual cycle may influence gastrointestinal symptomatology. However, hysterectomy has been reported to be performed for menstrual dysfunction and long before the advent of Rome III criteria for functional bowel disorders.

Many female patients report changes in their bowel patterns or worsening of their gastrointestinal symptoms in relationship to their menstrual cycles [4]. In one study

Fig. 1. Flowchart summarizing the selection process of patients. FGIDs, functional gastrointestinal disorders.

[4], gastrointestinal symptoms were looked for before and during menses in healthy women. There was no difference in the symptom of diarrhea during the premenstrual phase (24%) as compared to during menses (28%; $p = 0.44$). There was no difference either in the frequency of complaint of constipation. In contrast to this study [4], other authors performed a prevalence study on the effects of the menstrual cycle in inflammatory bowel disease and IBS [5]. They described equivalent (20%) rates of diarrhea and constipation premenstrually, but a reduction in both rates during menses. Yet they also demonstrated that there was less diarrhea in controls than in IBS patients during menstruations, as well as less constipation. These studies, taken together, may suggest that if menses exert an effect on bowel pattern, it is only in women with IBS, or with functional gastrointestinal disorders (FGIDs). Furthermore, these 2 studies do not use the Rome criteria to establish the diagnosis.

In addition, the report that mood disorders such as depression can be exacerbated premenstrually is well known [6]: 19% of American women have menstrual complaints and those with menstrual complaints are more likely to also have mood symptoms.

The aim of the present study was to search for a possible association between improvement of defecation with menses, FGIDs, and their mood and physiological correlates.

Patients and Methods

Subjects

From January 1, 2011 to December 31, 2014, 1,450 different outpatients (875 females) were referred to the gastrointestinal unit of the Avicenne Hospital, a tertiary center for FGID management.

Among them, 478 consecutive female outpatients in the reproductive age, with full evaluation, were included in the present study (Fig. 1). This retrospective study does not need ethical approval but was declared in the French National Agency for drug safety (ANSM, Agence Nationale de Sécurité du Médicament et des produits de santé, decision number: 2015-A01926-43). Patients were referred from a gastroenterologist or a general practitioner after an initial symptomatic treatment that failed or for diagnostic purposes before starting a treatment.

Before inclusion, a full evaluation of included patients ruled out any organic cause for their complaint. Patients with neurologic disease (stroke, spinal trauma, Parkinson disease, or multiple sclerosis) and patients with endocrine diseases (hypercalcemia or thyroid diseases) or autoimmune diseases (scleroderma, rheumatoid polyarthritis, other autoimmune diseases, or connective tissue disorders) were excluded. Patients with chronic use of NSAIDs (more than once per month) were also excluded. Diabetic patients were referred to the diabetes specialists when diabetes was poorly controlled. Intake of medications like calcium channel inhibitors were assessed at the initial evaluation and a switch to a different antihypertensive treatment from another pharmacological class was prescribed. If symptoms improved, patients were excluded from the study since complaints were considered to be a side effect of treatment. If symptoms remained, they were included in the study.

Patients also had morphological evaluation (endoscopy or radiology). Patients with anorectal symptoms and symptomatic hemorrhoids were excluded, patients with hemorrhoids that were not symptomatic (a very common finding) were included, but this was not registered in our database. Patients with anal fistula and abscess were also excluded. A gastric fibroscopy was performed in all patients with upper gastrointestinal disorders and patients with *Helicobacter pylori* infection were excluded.

Patients with a history of previous surgery of the gastrointestinal tract or drug or alcohol addiction were excluded from the study. A single investigator (M.B.) confirmed independently, during the medical visit, the validity of the initial diagnosis of FGID. In addition, all overweight patients who participated in a specific program for losing weight, use of gastric balloon, or bariatric surgery were excluded in order to avoid inducing any bias of selection. Finally, all patients who had a change of lifestyle (diet, physical activity) or drug treatment during the study were excluded.

Study Design

The current study is a retrospective observational study.

Clinical Questionnaires

Patients filled out a standard clinical questionnaire based on diagnostic questions for chronic FGIDs in the gastroenterologist's office during their visit. The interpretation was based on the functional disorders as defined by the Rome III criteria for functional esophageal disorders (heartburn, non-cardiac chest pain, dysphagia, globus), functional gastroduodenal disorders (dyspepsia, postprandial distress syndrome, epigastric pain syndrome, aerophagia), functional bowel disorders (IBS and its subtypes, bloating, constipation, diarrhea, and unspecified), functional abdominal pain, functional anorectal disorders (fecal incontinence, anorectal pain including levator ani syndrome, and proctalgia fugax), and difficult defecation.

In addition to the above-mentioned symptoms, stool description using the Bristol Stool Form Scale, regurgitation, soiling, and urinary (urinary incontinence, dysuria, pollakiuria) and sexual dysfunction (dyspareunia, impotence, pain during sexual intercourse) were recorded as previously described [7].

Finally, all the patients answered the question: “Have you had improvement of constipation before or during menses?” Improvement of constipation was defined by the improvement of at least 2 of the 6 symptoms used in the Rome III criteria to define constipation [8]: (i) decrease of straining during defecation, (ii) softer stools, (iii) decrease of the sensation of incomplete evacuation, (iv) decrease of the sensation of anorectal obstruction/blockage, (v) decrease of the frequency of manual maneuvers to facilitate defecation, and (vi) increase of the number of defecations per week. The questionnaires were filled in independently of the follicular or luteal menses phases.

Self-Evaluation of Symptoms

Patients filled in a 10-point (0–9) Likert scale to evaluate the intensity of 4 digestive symptoms: constipation, diarrhea, abdominal bloating, and abdominal pain (for pain, 0 is no pain, 9 is the most severe pain). They were asked to score the symptoms experienced during the previous month.

Psychometric Evaluation

Psychometric evaluation was focused on anxiety and depression. The level of depression was assessed by the Beck Depression Inventory (BDI II), frequently used in the evaluation of depression in gastrointestinal pathologies. It contains 21 multiple-choice items with a score from 0 to 3 each, so that the total point score varies from 0 to 63. All subjects completed the French validated translation of the BDI-II [9]. Anxiety was assessed by the French validated translation of the State and Trait Anxiety Inventory (STAI), made up of 2 axes (A1 for state anxiety and A2 for trait anxiety), both consisting of 20 multiple-choice items; each item has a score from 1 to 4 so that the total point score of the A1 and A2 axes can range from 20 to 80 and also because it was used to evaluate anxiety levels and to distinguish “state” anxiety from “trait” anxiety in gastrointestinal diseases [10]. The test is based on the conceptual distinction between anxiety as a transitory “state,” expressed by emotional reactions of different degrees, and anxiety as a relatively stable personality “trait”. “State” anxiety is conceptualized as an emotive “state” characterized by subjective feelings perceived on a conscious level, such as apprehension and tension, which vary with time; anxiety as a “trait” refers to individuals with a continuous disposition towards anxiety [10].

Physiological Evaluation

All physiological tests started at least 1 week after the end of the menstrual phase.

Measure of Total and Segmental Colonic Transit Time

The measure of colonic transit time (CTT) was performed before the study by using the technique we previously described [11]. Briefly, twelve radiopaque markers within a gelatin capsule were ingested at 9:00 a.m. from day 1 to 6. A plain film of the abdomen was taken on the seventh day, at 9:00 a.m. Markers were localized and counted in the different segments of the large bowel according to bony landmarks [11]. Three zones of interest were defined for the measurement of segmental CTT: the right colon, the left colon, and the rectosigmoid area [12]. Segmental and total colorectal transit times were calculated according to the distribution of markers in the different segments of bowel over successive days. This was done according to the equation: $CTT_i = n_i DT/N$, where CTT_i is the mean transit time of a single marker in region i , n_i is the number of markers found in the studied zone i , DT is the time interval between 2 consecutive ingestions of markers ($T = 24$ h), and N is the number of markers ingested every day ($n = 12$). Total CTT was the sum of the 3 segmental CTTs. Normal values of colorectal transit were previously established at between 24 and 65 h. The

compliance to markers ingestion was assessed by rigorous instruction before study and the systematic examination of a diary. All digestive drugs used for the treatment of constipation were stopped 1 week before the measurement.

Anorectal Manometry

Patients underwent conventional anorectal manometry using perfused catheter, followed by a study of the volumes of sensation. Resting pressures were recorded in the rectal lumen and in the upper and lower anal canal. Six parameters were measured: 3 pressures (rectal, upper, and lower anal canal pressure), 3 rectal volumes (threshold sensation volume, constant sensation volume, maximum tolerable volume).

Anismus was defined as a rise of at least 10 mm Hg in anal canal pressure during straining, reproduced 3 times during 3 episodes of straining efforts. A second criterion had to be present: the subjects had to fail to expel the rectal balloon filled with 30 mL of water at room temperature before straining.

Statistical Analysis

Statistical analyses were carried out using IBM SPSS (IBM SPSS Statistics version 20). The results are expressed as mean $\pm$ standard deviation. Chi-square tests were used for analysis of qualitative variables. Categorical differences among the groups were analyzed by one-way analysis of variance (ANOVA). Multiple comparisons with post hoc tests using Bonferroni correction were used if ANOVA showed significant differences. As we employed multiple statistical testing, we have adjusted the level to <0.01 rather than 0.05. Whenever multiple tests are employed in a nonexperimental paradigm, there is an increased risk of type I (false positive) error. Hence, we interpret statistically significant findings in this study as evidence of an association rather than definitive proof of an association.

Logistic regression was used for data analysis, which included systematically as independent variables: age, body mass index, functional bowel disorders, Bristol stool form scale scores, self-evaluation of the symptoms, the 3 psychological scale scores (BDI-II, A1, A2), total and segmental CTT, and anorectal manometric parameters as dependent variable. The backwards selection procedure was used for model selection during multivariate logistic regression. Only statistically significant variables ($p < 0.01$) remained in the adjusted model.

Results

The 478 women included in the present study were between 18 and 50 years old (35.2 ± 9.0 years); their body mass index was between 18 and 37.2 (26.6 ± 7.0). The duration of the disorder ranged between 5 and 18 years. These patients had 1.3 ± 1.2 children, 134 patients (28%) were nulliparous, and 205 patients (43%) were sedentary without any physical activity and were unemployed or retired.

The clinical results of the present study are summarized in Table 1, and the physiological results are shown in Table 2. Extra-bowel disorders were found in 65% of patients: 34% reported esophageal disorders, 28% reported gastroduodenal disorders, and 38% reported anorectal disorders.

Table 1. Comparison of demographic, psychological, clinical, and physiological parameters according to the presence of improvement of defecation related to menses

	All female patients	No improvement	Improvement	<i>p</i> value
<i>Demographics</i>				
Number (%)	478 (100)	381 (80)	97 (20)	<0.001
Age, years	35.2±9.0	35.8±9.1	32.9±8.3	0.005
Body mass index	26.6±7.0	26.6±7.2	26.6±6.4	0.973
<i>Psychological</i>				
Depression	14.5±10.8	14.6±10.7	14.1±11.0	0.686
State anxiety (A1)	41.1±13.3	41.2±13.4	40.8±13.3	0.772
Trait anxiety (A2)	44.2±11.5	44.0±11.5	45.0±11.7	0.445
<i>Digestive disorders</i>				
Esophageal				
Globus	88 (18)	74 (19)	14 (14)	0.039
Regurgitation	51 (11)	40 (10)	11 (11)	0.576
Chest pain	119 (25)	91 (24)	28 (29)	0.963
Heartburn	152 (32)	120 (31)	32 (33)	0.886
Dysphagia	98 (21)	75 (20)	23 (24)	0.595
Gastroduodenal				
Epigastric pain	37 (8)	31 (8)	6 (6)	0.613
Postprandial distress	89 (19)	77 (20)	12 (12)	0.110
Dyspepsia	115 (24)	87 (23)	28 (29)	0.464
Aerophagia	114 (24)	86 (23)	28 (29)	0.428
Bowel				
IBS (all subtypes)	179 (37)	141 (37)	38 (39)	0.364
IBS with constipation	64 (13)	43 (11)	21 (22)	<0.001
IBS with diarrhea	53 (11)	47 (12)	6 (6)	0.072
Mixed IBS	35 (7)	30 (8)	5 (5)	0.464
Unsubtyped IBS	27 (6)	21 (6)	6 (6)	0.758
Constipation	91 (19)	67 (18)	24 (25)	0.244
Diarrhea	45 (9)	39 (10)	6 (6)	0.134
Bloating	28 (6)	22 (6)	6 (6)	0.567
Nonspecific bowel disorders	38 (8)	28 (7)	10 (10)	0.725
Functional abdominal pain	29 (6)	27 (7)	2 (2)	0.123
Anorectal				
Soiling	32 (7)	29 (8)	3 (3)	0.037
Fecal incontinence	30 (6)	28 (7)	2 (2)	0.027
Levator ani syndrome	24 (5)	21 (6)	3 (3)	0.657
Proctalgia fugax	33 (7)	23 (6)	10 (10)	0.069
Obstructed defecation	159 (33)	132 (35)	27 (28)	0.050
<i>Extradigestive disorders</i>				
Urological	96 (20)	80 (21)	16 (16)	0.279
Sexological	77 (16)	65 (17)	12 (12)	0.592
<i>Likert scales</i>				
Bristol Stool Form	3.6±1.9	3.7±1.9	3.0±1.6	0.001
Constipation	3.0±3.2	2.9±3.2	3.2±2.9	0.436
Diarrhea	1.9±2.7	2.1±2.8	1.2±2.0	0.007
Bloating	4.1±3.1	4.2±3.1	3.7±3.0	0.173
Abdominal pain	3.9±3.1	4.0±3.2	3.5±2.9	0.177

Quantitative parameters are shown as mean ± standard deviation, qualitative parameters are shown as *n* (%). IBS, irritable bowel syndrome.

Table 2. Comparison of physiological parameters according to the presence of improvement of defecation related to menses

	All female patients (<i>n</i> = 478)	No improvement (<i>n</i> = 381)	Improvement (<i>n</i> = 97)	<i>p</i> value
Anorectal manometry				
Rectal pressure, mm Hg	21.8±28.8	21.0±26.5	29.0±42.8	0.114
Upper anal pressure, mm Hg	38.4±26.2	38.8±27.0	34.9±18.6	0.402
Lower anal pressure, mm Hg	54.6±31.5	54.4±30.1	56.0±41.7	0.768
Threshold perception volume, mL	60.2±36.9	62.0±37.4	45.6±28.8	0.011
Constant sensation volume, mL	112.8±60.0	115.5±61.8	90.8±36.1	0.019
Maximum tolerable volume, mL	212.3±102.7	215.5±106.0	186.1±65.3	0.105
Anismus	167 (35)	133 (35)	34 (35)	0.886
Colonic transit time				
Oroanal transit time, h	49.1±37.3	46.5±35.3	58.8±42.8	0.001
Right colon transit time, h	16.1±18.0	15.9±18.6	16.5±15.6	0.771
Left colon transit time, h	17.5±18.6	16.3±17.6	21.9±21.3	0.003
Rectosigmoid transit time, h	15.6±17.0	14.3±15.5	20.7±20.8	<0.001

Quantitative parameters are shown as mean ± standard deviation, qualitative parameters are shown as *n* (%).

Ninety-seven (20%) female patients reported easier defecation associated with menses. These patients are younger ($p = 0.005$) but have similar body mass indices and psychological profiles (depression, state and trait anxiety) than the other women. Clinically, they reported more frequently IBS with constipation ($p < 0.001$) and had harder stools ($p = 0.001$), but they also scored higher on diarrhea as defined by the Likert scale ($p = 0.007$). Interestingly, they complained less often of globus ($p = 0.039$) but not of anismus at the lower extremity of the gastrointestinal tract.

Physiologically, these patients had delayed oroanal transit time ($p < 0.001$), with delayed left colonic ($p = 0.003$) and rectosigmoid transit time ($p < 0.001$).

In these patients, the logistic regression confirmed the association of easier defecation related to menses with lower age ($p < 0.001$; OR 0.952; 95% CI 0.926–0.978), IBS with constipation ($p = 0.007$; OR 2.812; 95% CI 1.326–5.960), proctalgia fugax ($p = 0.008$; OR 3.417; 95% CI 1.378–8.475), hard stools ($p = 0.005$; OR 0.805; 95% CI 0.692–0.936), and delayed left CTT ($p = 0.002$; OR 1.013; 95% CI 1.002–1.024).

Discussion

The present study shows that in female FGID patients, improvement of defecation with menses is associated with a younger age, IBS-constipation phenotype, proctalgia fugax, and report of hard stools. Physiologically, these patients have delayed transit in the left colon. In contrast, no association with mood parameters or anorectal manometric characteristics were found in these patients.

Gastrointestinal symptoms have been reported to vary with the menstrual cycle: 64% had change in bowel habits during menses [13], one-third of asymptomatic women may experience gastrointestinal symptoms at the time of menstruation, and almost 50% of women with IBS report a perimenstrual increase in symptoms [14] and harder stools during the luteal phase of the menstrual cycle [15].

The main criterium of analysis in the present study was an improvement in defecation related to menses, and it is not surprising to find that the women who report such improvement have harder stools outside of menstruations. The frequency of this report in the present study (20%) is lower than in a previous study where approximately one-third of females reported some change in stool consistency during menstruation [16]. However, the results of the present study differ from those of a Japanese study that found immediately before menstruation, in constipated women, feces to become harder and looser in 22.1 and 13.7%, respectively, compared with 8.7 and 9.5% in normal women [17].

The report of a higher frequency of stomach pain, pelvic cramping, nausea, and diarrhea at menses in the IBS patients was previously described, in favor of an enhancement of visceral sensitivity during the perimenstrual period [18]. In addition to the higher prevalence of visceral pain in women during the perimenstrual phase, it has been shown that a diagnosis of IBS was 3 times more common in women with painful menstruation than in those without [19] and a meta-analysis has shown that women with IBS as well as healthy women reported an increase of IBS symptomatology during menses as compared with other phases [20]. In IBS patients, bloating was also associated with uterine cramping and breast

tenderness but not with constipation [21]; however, in the present study the association of improvement of constipation during menses was only found in the IBS-constipation group.

The only study focusing on the interaction of menstrual cycle with FGIDs has shown that gastrointestinal symptoms are frequent (73%) either before or during menses, with abdominal pain (58% pre; 55% during) and diarrhea (24% pre; 28% during) being the most common ones and related to depression and anxiety [4]. However, abdominal pain is difficult to separate from pelvic pain because, in contrast to somatic pain, visceral pain is generally vague, poorly localized, and characterized by hypersensitivity to stimuli such organ distension [22]. Thus, the most reliable symptom of an association of gastrointestinal symptoms with menses ought to be an improvement of defecation associated with menses.

Clinical studies have shown that depression and anxiety can influence the feeling and the severity of digestive symptoms in a large number of FGIDs such as IBS [23], but it remains unknown whether women who experience emotional symptoms around menses are more likely to have concomitant digestive symptoms. Nevertheless, there are few studies which have assessed whether there is a relationship between mood and FGIDs around menses in women [23]. In the present study, proctalgia fugax was associated with improvement of defecation with menses, but the literature does not report such association.

The association of hormonal levels and change in colonic motor functions was assessed by colonic and anorectal motility, intestinal transit time and CTT, or frequency of bowel movements, but the results of these studies are conflicting.

Some studies stated that CTT is uniformly the same in both genders [24], while other studies found that oro-caecal transit time [25], total CTT [15], or rectosigmoid transit time [26] were found to be significantly prolonged in the luteal phase and were increased compared with the follicular phase, while other studies found no significant change of the oro-caecal [27] or the oro-anal [28] transit time between the follicular phase or in the luteal phase.

Despite the high prevalence of female gender in IBS and constipation, some studies found no gender difference in colonic motor function [29]. However, *in vivo* and *in vitro* animal experiments [30] have suggested that female steroid hormones can affect gastrointestinal motility [31].

Changes in rectal motility and therefore a change in the bowel pattern during menstruation are also discordant: changes with menses [16] or no effect as shown by other authors [32]. Physiologically, no significant differences were found in the detection of estrogen and progesterone receptors in structures of the anal canal in women

in relation to menopausal status and age, despite the fact that this organ is a target for sex steroid hormones.

The frequency of bowel movements increases with age in males but not in females [16]. The influence of younger age on changes in bowel pattern (i.e., soft stool associated with their menstrual cycle) was previously reported by keeping the younger females in one group and the postmenopausal females in another [16]. The present study shows that, in non-menopausal women, younger age is also a factor of improvement of defecation with menses.

In a small group of menstruating women, it was shown that an increase in stool frequency was associated with an increase in dietary fiber intake at the time of the bleeding [33]. However, dietary intake that could be associated with FGIDs [34, 35] was not recorded in the present study.

Functional gastroenterological problems are more common in females than in males. This is attributed to many factors including psychological distress. It is difficult to evaluate psychological symptoms through a questionnaire and we were not able to make any statement attributing change in bowel function related to any psychological factor [23]. In some studies, no significant effect of cycle on self-reports of anxiety or depression was found, while in other studies, anxiety and depression were risks factors of digestive symptoms in association with the premenstrual and menses phases [4]. In the present study, improvement of constipation with menses was not associated with mood disorders.

To conclude, improvement of defecation with menses is mainly associated with IBS with constipation, proctalgia fugax, lower age, and hard stools and not associated with functional constipation, depression, anxiety, or functional anorectal parameters.

Statement of Ethics

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all patients.

Disclosure Statement

M.B., G.D., F.M., P.R., B.B., and R.B. have no competitive interests.

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Author Contributions

M.B. performed the research, contributed to the design of the study, performed data analysis, participated in the interpretation of data, wrote the article, revised the article for its content, and approved its final version. G.D. revised the article for its content and approved its final version. P.R. participated in the selection of

the patients and revised the article for its content. F.M. participated in the selection of the patients and revised the article for its content. B.B. participated in the selection of the patients and revised the article for its content. R.B. participated in the selection of the patients, contributed in the design of the study, revised the article's content, and gave final approval for the version to be published.

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