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Increased Symptoms in Female IBS Patients With Dysmenorrhea and PMS

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Women with irritable bowel syndrome often report premenstrual distress syndrome and dysmenorrhea. A descriptive, four-group comparison design was used to compare the symptoms and psychological distress levels of women with irritable bowel syndrome (age 18–45 years) with and without dysmenorrhea and premenstrual distress syndrome. Data from three studies on women with irritable bowel syndrome (n = 226) collected between 1995 and 2004 were combined. Of these, 38 had self-reported irritable bowel syndrome with dysmenorrhea and premenstrual distress syndrome, 59 had irritable bowel syndrome with premenstrual distress syndrome, 15 had irritable bowel syndrome and dysmenorrhea, and the remaining 114 had irritable bowel syndrome only.

Participants completed the Symptom Checklist-90 Revised and a symptom diary. Pain symptoms and computed scales of anxiety, depression, anger, and cognitive difficulties were compared during the luteal phase, menses phase, and for the change from luteal to menses phases. Premenstrual distress syndrome and dysmenorrhea had a strong impact on uterine cramping at menses, and a weaker effect on other pain symptoms at both luteal and menses phases. Premenstrual distress syndrome was associated with higher depression, anger, and cognitive problems at both luteal and menses phases; however, it was not associated with a greater increase from luteal to menses phases for any symptoms other than uterine cramping. The multiple symptoms reported by women with both irritable bowel syndrome and premenstrual distress syndrome suggest that this group may be particularly challenging to treat and may require a multicomponent (e.g., education, diet, relaxation, cognitive restructuring) approach.

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Approximately 9–17% of American women report chronic gastrointestinal (GI) symptoms compatible with a diagnosis of irritable bowel syndrome (IBS; Drossman et al., 1993; Thompson, Irvine, Pare, Ferrazzi, & Rance, 2002). In conjunction with key GI symptoms (i.e., abdominal pain, changes in stool consistency and frequency) associated with this disorder, women with IBS often report a number of other somatic and visceral symptoms collectively referred to as "extra-

intestinal" symptoms of IBS (Lee, Mayer, Schmulson, Chang, & Naliboff, 2001). Of these, dysmenorrhea and perimenstrual syndrome (PMS) are among the most common.

In a cross-sectional study of 987 women attending a pelvic pain clinic, Williams, Hartmann, Sandler, Miller, and Steege (2004) found that 35% of participants met the Rome I criteria for IBS. Lea, Bancroft, and Whorwell (2004) noted 30% of participants with gynecologic pathology (e.g., endometriosis) also reported symptoms suggestive of IBS. Using a large health maintenance organization database, Longstreth and Yao (2004) recently reported women with IBS were twice as likely to experience a hysterectomy as women without IBS, confirming gynecologic symptoms have a high prevalence in women with IBS.

Dysmenorrhea or painful uterine cramping pain co-occurs in 25–50% of women with IBS. Premenstrual distress syndrome (PMS), defined as emotional and physical changes prior to menses, is also estimated to occur in approximately 20–50% of women with IBS (Heitkemper et al., 2003; Whitehead, Palsson, & Jones, 2002). For women who have dysmenorrhea, PMS, and IBS, symptoms tend to worsen in the luteal and early menses phases (Heitkemper et al., 2003, 2004; Whitehead et al.). Several studies have demonstrated that women with dysmenorrhea have greater pain sensitivity, particularly at menses, as compared to women without dysmenorrhea (Bajaj, Bajaj, Madsen, & Arendt-Nielsen, 2002; Giamberardino, Berkley, Iezzi, deBigontina, & Vecchiet, 1997; Heitkemper et al., 2004; Riley, Robinson, Wise, & Price, 1999). Similarly, women with IBS express greater sensitivity to rectal distention compared to women without IBS, particularly at menses (Houghton, Lea, Jackson, & Whorwell, 2002).

In addition to the overlap of symptoms and the menstrual cycle-linked amplification of symptoms, dysmenorrhea, PMS, and IBS are also associated with increased psychological distress as measured both prospectively and retrospectively by Sigmon, Whitcomb-Smith, Rohan, and Kendrew (2004), Walsh, LeBlanc, and McGrath (2003), and Wang et al. (2004). Despite the documented coexistence of dysmenorrhea and/or PMS with IBS, these conditions have been studied primarily as separate entities and thus, there is little to no information available on their combination. It remains to be determined whether women with IBS who report concurrent PMS or dysmenorrhea have higher levels of psychological distress.

The current study tested the hypothesis that women who report dysmenorrhea and/or PMS in addition to IBS will also report more severe or frequent symptoms than women with IBS alone, in the luteal phase and at menses.

Materials and Methods

Sample

This report is a secondary analysis of data collected from three descriptive studies on women with and without IBS. The aims of these three initial studies were (i) to assess autonomic nervous system function (IBS, $n = 111$; controls, $n = 48$); (ii) to test the effectiveness of a cognitive-behavioral treatment (IBS, $n = 59$); and (iii) to describe immune function across the menstrual cycle (IBS, $n = 56$; controls, $n = 65$). In each of the three studies, women were recruited through community advertisement except for 58 women with IBS who were recruited through a direct mailing from a health maintenance organization. Only data from women with IBS were used in the statistical analyses.

To be eligible for these analyses, women needed to have regular menstrual cycles, be of age 18–45 years with a diagnosis of IBS by a healthcare provider, and have current GI symptoms indicative of IBS (Thompson et al., 1999). Comorbid organic GI and reproductive health conditions were exclusionary. All data were collected between 1995 and 2004. Each of the three studies and the combined data analyses were approved by Human Subjects Institutional Review Board.

Measures

Demographic information was obtained including age, marital status, education, ethnic affiliation, occupation, and medication use. Women were asked to complete questionnaires during the initial interview. Dysmenorrhea was assessed during the interview by asking the women "Are your periods more painful than those of most women you know?" PMS was determined with the question "Do you have PMS (premenstrual syndrome), that is, the appearance of marked mood changes or irritability the week before you period?" If yes, "How much of a problem is this for you?" was rated as "mild," "moderate," or "severe." For this analysis, a score of "moderate" or "severe" was rated as positive for PMS and the remainder was scored as non-PMS.

Symptom Checklist-90 Revised

The Symptom Checklist-90 Revised (SCL-90R) includes 90 items that measure psychological distress (Derogatis, 1994; Derogatis & Cleary, 1977). For this study, the Global Severity Index (GSI; mean of all 90 items) and the depression and anxiety subscales are reported. Participants were asked to rate how much the symptom distressed or bothered them for the prior seven days on a scale from "not at all" = 0 to "extremely distressing" = 4. Acceptable indicators of validity and reliability have been described. The internal consistency of the GSI was $\alpha = .97$ in this study.

Daily Diary

Participants completed a symptom diary each evening for one menstrual cycle plus days 1–5 of the next menses. The severity of each of 51 symptoms was rated every evening in the daily diary, on a scale going from 0 (not present) to 4 (extreme). Six scales were computed by averaging several symptoms. The scales were "depression" (feeling depressed, decreased desire to talk or move, hopelessness, and loneliness), "anxiety" (anxiety, nervous-jittery, panic feelings, and out of control or overwhelmed), "anger" (anger, hostility, impatient, and irritable), "sleep problems" (hard to fall asleep, waking up during the night, waking up too early), "cognitive" (forgetfulness, hard to concentrate, hard to make decisions), and "somatic symptoms" (backache, headache, joint and muscle pain). Only women who completed the daily diary for the total cycle were included in the analyses. Analyses were done on six individual pain symptoms (uterine cramping, abdominal pain, stomach pain, backache, joint or muscle pain, headache) and the six symptom scales.

Statistical Analyses

Patients with IBS were classified into one of four categories: IBS with both dysmenorrhea (DYS) and PMS (IBS + PMS + DYS), IBS with PMS only (IBS + PMS), IBS with dysmenorrhea only (IBS + DYS), and IBS only (IBS-only). Symptoms

from the daily diary were categorized into early luteal (7–10 days prior to the onset of the menstrual cycle) and menses (first day of menses). The period 7–10 days prior to menses was chosen because it was well before the premenses rise in symptoms and hence represents the non-perimenses portion of the menstrual cycle.

Analysis of variance was used to test whether the four groups differed on symptom severity, separately at the luteal and menses phases. In addition, a change score was computed as the change from the luteal to menses phase and analyzed with analysis of variance. As some women were using oral contraceptives, the analysis of variance model also included oral contraceptive use as a factor.

Results

Two-hundred twenty-six women with IBS were included in the study. On average, the participants were 32 years of age, predominantly Caucasian (87%), and about half were married or partnered. Most women had completed college and held professional or managerial jobs. Approximately half (n = 114, 51%) of the women had neither PMS nor dysmenorrhea (IBS-only), 15 (7%) had IBS and dysmenorrhea (IBS + DYS), 59 (26%) had IBS and PMS (IBS + PMS) and 37 (16%) had all three (IBS + PMS + DYS). Sixty-five (29 %) of the women had taken oral contraceptives during the study.

Symptoms

As shown in Figure 1, all groups reported increased uterine cramping around menses, peaking on the first day of menses (for graphical comparison purposes only, data from a group of non-IBS women [controls] are shown in Figures 1 and 2). This trend also appears, though not nearly as strong, for most of the other pain symptoms and is also reflected in the somatic scale in Figure 2, which is the average of the pain symptoms headache, backache, and joint or muscle pain.

Group differences for pain symptoms are shown in Table 1. The most significant group differences are for uterine

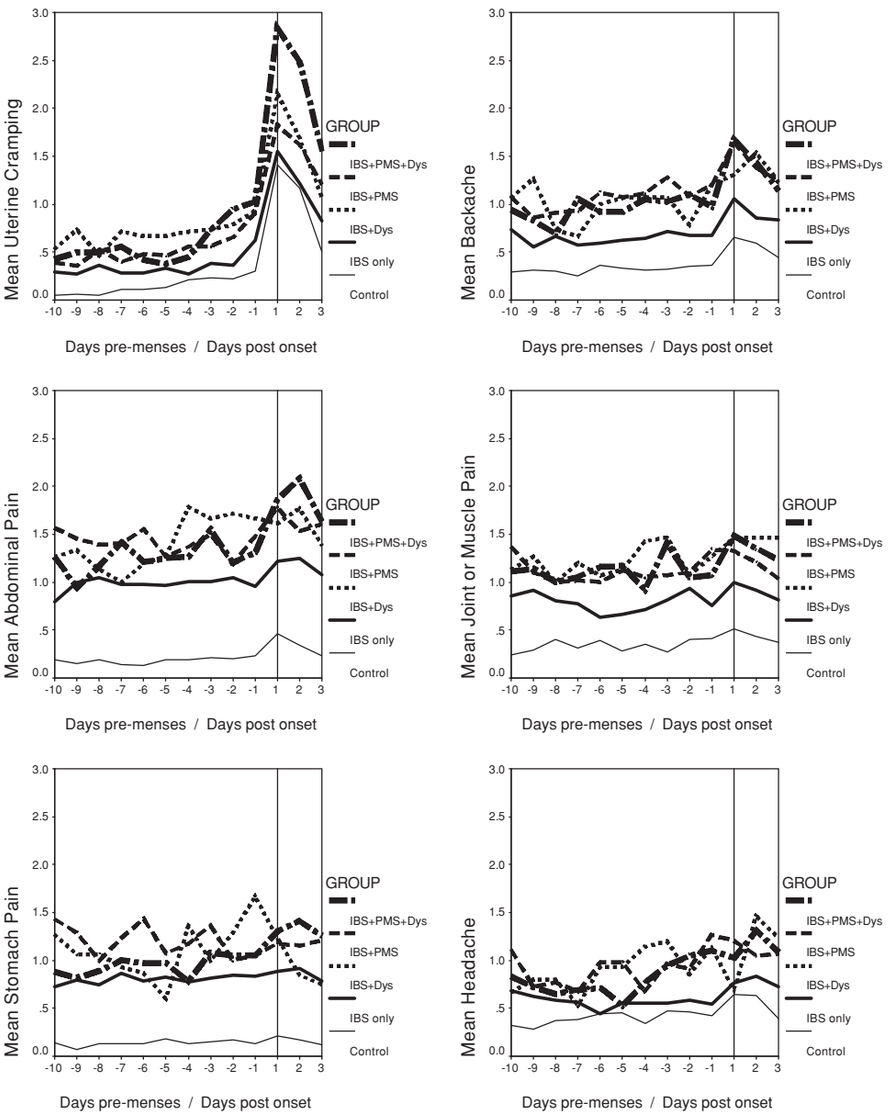

FIGURE 1. Daily pain symptom intensity ratings for women with IBS-only (n = 114), IBS + DYS (n = 15), IBS + PMS (n = 59), IBS + DYS + PMS (n = 37). Only luteal phase (days −10 to −1) and menses phase (days 1–3) days are shown. Symptoms were rated from 0 (not present) to 4 (extreme).

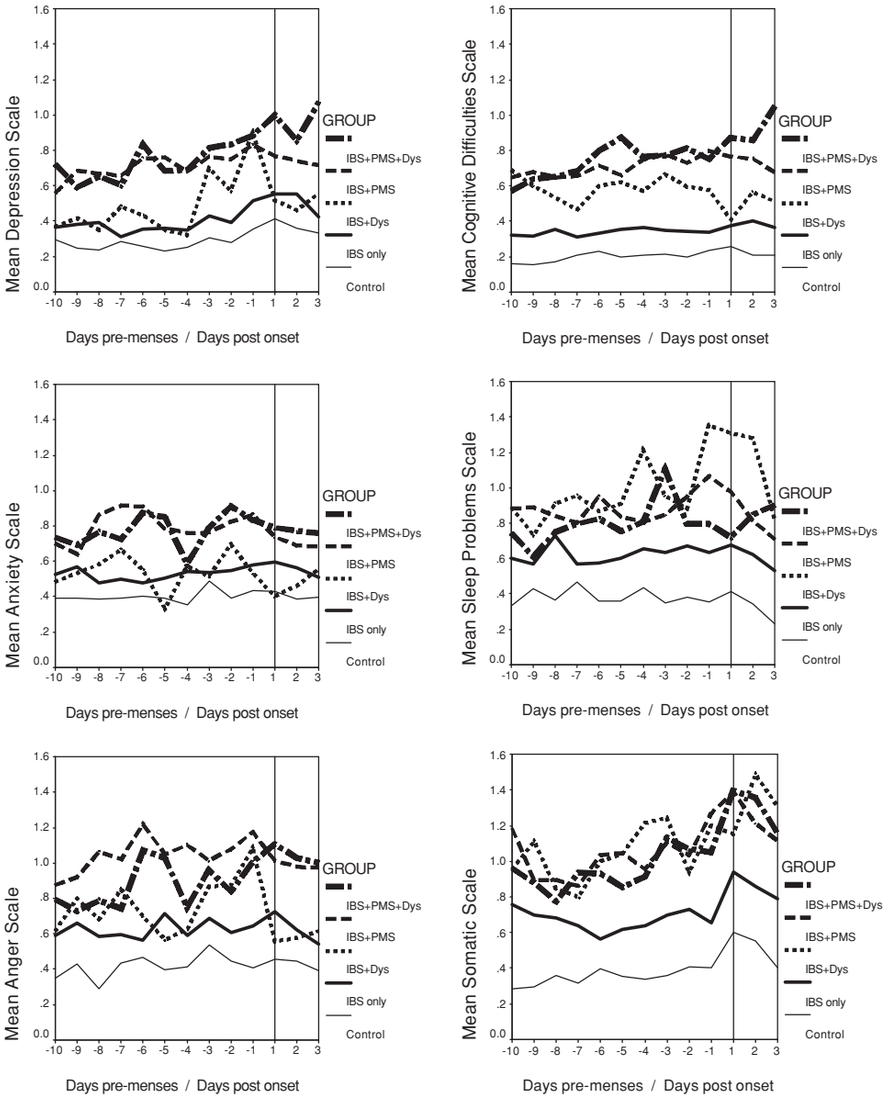

FIGURE 2. Daily psychological distress, sleep, and somatic complaint scale ratings for women with IBS-only ($n = 114$), IBS + DYS ($n = 15$), IBS + PMS ($n = 59$), IBS + DYS + PMS ($n = 37$). Only luteal phase (days –10 to –1) and menses phase (days 1–3) days are shown. Symptoms were rated from 0 (not present) to 4 (extreme).

cramping at menses and the change from luteal to menses phases. The IBS + PMS + DYS group has the greatest uterine cramping at menses. None of the other pain symptoms show a significant difference across groups in the change from luteal to menses phases, though some show marginally significant group differences at both luteal and menses phases.

Figure 2 and Table 2 show means by group of the six symptom scales. The strongest group differences are seen for depression, anger, and cognitive difficulties, all of which are significant at both luteal and menses phases. In general, the two groups with PMS have worse symptoms than the IBS-only group. None of the scales show a significant difference across groups in the change from luteal to menses phases. Table 3 shows a very strong group effect for psychological distress as measured by the SCL-90R, with the two groups with PMS having worse psychological distress than the IBS-only group.

Discussion

Dysmenorrhea and/or PMS were reported by almost half of the IBS women with the highest percentage of these reporting IBS + PMS. PMS and dysmenorrhea had a strong impact on uterine cramping at menses, less so on other pain symptoms. PMS was associated with higher depression, anger, and cognitive problems at both luteal and menses phases; however, it was not associated with a greater increase from luteal to menses phases for any symptoms other than uterine cramping.

The results of this study have implications for the study of women with IBS. In the United States as well as in other western industrialized countries, more women than men seek healthcare services for symptoms compatible with a diagnosis of IBS (Drossman et al., 1993). As a result, women are disproportionately represented in clinical and laboratory studies of IBS. Although it has been established that women with IBS

TABLE 1

Effects of Pain/Discomfort Symptoms on Groups During Luteal Phase (Days 7–10 Prior to Onset of Menses) and Menses (Onset/First Day of Menses), and the Difference (Change From Luteal to Menses Phases)

Symptoms	Subgroups	Luteal, Mean (*SD*)	Menses, Mean (*SD*)	Difference, Mean (*SD*)
Uterine cramping	IBS + PMS	0.42 (0.65)	1.83 (1.40)	1.42 (1.39)
	IBS + DYS	0.63 (0.91)	2.15 (1.46)	1.60 (1.72)
	IBS-only	0.30 (0.59)	1.55 (1.32)	1.24 (1.33)
	Group effect	*ns*	< .001	.002
Abdominal pain	IBS + PMS + DYS	1.13 (0.81)	0.77 (0.74)	–0.36 (0.84)
	IBS + PMS	1.31 (0.90)*	0.70 (0.64)	–0.62 (0.86)
	IBS + DYS	1.06 (0.87)	0.82 (0.87)	–0.25 (0.87)
	IBS-only	0.89 (0.78)	0.50 (0.58)	–0.39 (0.69)
	Group effect	.02	.06	.18
Stomach pain	IBS + PMS + DYS	0.86 (0.90)	1.31 (1.12)	0.44 (1.10)
	IBS + PMS	1.22 (1.00)*	1.17 (1.29)	–0.03 (1.04)
	IBS + DYS	1.08 (1.02)	1.23 (1.30)	0.37 (0.96)
	IBS-only	0.78 (0.84)	0.89 (1.11)	0.07 (0.87)
	Group effect	.03	.19	.14
Backache	IBS + PMS + DYS	0.87 (0.93)	1.68 (1.41)*	0.81 (1.05)
	IBS + PMS	0.93 (1.03)	1.64 (1.35)*	0.66 (1.12)
	IBS + DYS	0.93 (0.90)	1.31 (1.38)	0.42 (1.37)
	IBS-only	0.62 (0.73)	1.05 (1.06)	0.43 (0.99)
	Group effect	.13	.02	*ns*
Joint or muscle pain	IBS + PMS + DYS	1.07 (1.04)	1.49 (1.39)	0.41 (1.04)
	IBS + PMS	1.10 (1.07)	1.33 (1.23)	0.18 (1.20)
	IBS + DYS	1.15 (1.19)	1.46 (1.45)	0.38 (0.89)
	IBS-only	0.82 (0.92)	1.00 (1.18)	0.17 (0.98)
	Group effect	*ns*	*ns*	*ns*
Headache	IBS + PMS + DYS	0.71 (0.84)	1.03 (1.46)	0.32 (1.28)
	IBS + PMS	0.80 (0.96)	1.21 (1.40)	0.38 (1.22)
	IBS + DYS	0.70 (0.66)	0.69 (1.32)	–0.04 (1.06)
	IBS-only	0.61 (0.78)	0.77 (0.99)	0.17 (0.94)
	Group effect	*ns*	.17	*ns*

Note. IBS + PMS + DYS ($n = 38$); IBS + PMS ($n = 59$); IBS + DYS ($n = 15$); IBS-only ($n = 114$).

ns: $p > .20$.

*Significant differences ($p < .05$) between IBS-only and other groups.

are more likely to report additional extra-intestinal symptoms including those related to reproductive problems (e.g., PMS, dysmenorrhea, and dyspareunia; Fass, Fullerton, Naliboff, Hirsh, & Mayer, 1998), this is the first study to examine the impact of these coexisting conditions on day-to-day symptom reporting by women with IBS.

The results of our study clearly demonstrate that the presence of PMS alone or in combination with dysmenorrhea in women with IBS is associated with an amplification of symptom reports during the luteal as well as the menses phases of the menstrual cycle. Thus, it is important to consider the coexistence of other conditions that may influence symptom severity and menstrual cycle phase in evaluating treatment response. For example, the treatment of PMS with antidepressants that have anticholinergic properties may further exacerbate symptoms in women with constipation-predominant IBS.

Although the exact etiology of primary dysmenorrhea remains to be clarified, prostaglandins appear to play a prominent role in mediating uterine contractions. Using daily symp-

TABLE 2

Effects of Psychological Distress on Groups During Luteal Phase (Days 7–10 Prior to Onset of Menses) and Menses (Onset/First Day of Menses), and the Difference (Change From Luteal to Menses Phases)

Symptoms	Subgroups	Luteal, Mean (*SD*)	Menses, Mean (*SD*)	Difference, Mean (*SD*)
Depression	IBS + PMS + DYS	0.68 (0.71)*	1.00 (1.05)*	0.35 (0.84)
	IBS + PMS	0.64 (0.66)*	0.76 (0.92)	0.12 (0.76)
	IBS + DYS	0.40 (0.58)	0.52 (0.41)	0.28 (0.41)
	IBS-only	0.37 (0.47)	0.55 (0.76)	0.18 (0.68)
	Group effect	.003	.05	*ns*
Anxiety	IBS + PMS + DYS	0.74 (0.73)	0.79 (0.92)	0.05 (0.70)
	IBS + PMS	0.78 (0.70)*	0.74 (0.76)	–0.06 (0.50)
	IBS + DYS	0.57 (0.64)	0.40 (0.69)	–0.06 (0.50)
	IBS-only	0.51 (0.60)	0.60 (0.78)	0.06 (0.73)
	Group effect	.05	*ns*	*ns*
Anger	IBS + PMS + DYS	0.79 (0.65)	1.11 (0.93)	0.32 (0.85)
	IBS + PMS	0.97 (0.70)*	1.01 (0.92)	0.03 (1.00)
	IBS + DYS	0.74 (0.65)	0.56 (0.61)	–0.01 (0.75)
	IBS-only	0.60 (0.55)	0.72 (0.81)	0.11 (0.76)
	Group effect	.002	.03	*ns*
Sleep problems	IBS + PMS + DYS	0.71 (0.80)	0.72 (1.01)	0.01 (0.73)
	IBS + PMS	0.84 (0.79)	0.98 (1.04)	0.14 (0.85)
	IBS + DYS	0.87 (0.70)	1.31 (1.31)	0.44 (0.96)
	IBS-only	0.61 (0.65)	0.67 (0.93)	0.06 (0.81)
	Group effect	.20	.07	*ns*
Somatic symptoms	IBS + PMS + DYS	0.88 (0.79)	1.40 (1.15)*	0.51 (0.73)*
	IBS + PMS	0.94 (0.81)*	1.39 (0.97)*	0.41 (0.80)
	IBS + DYS	0.93 (0.77)	1.15 (1.19)	0.26 (0.87)
	IBS-only	0.68 (0.60)	0.94 (0.80)	0.26 (0.68)
	Group effect	.126	.023	*ns*
Cognitive	IBS + PMS + DYS	0.64 (0.71)*	0.87 (0.98)*	0.23 (0.72)
	IBS + PMS	0.66 (0.77)*	0.77 (1.00)*	0.11 (0.86)
	IBS + DYS	0.57 (0.71)	0.41 (0.51)	0.01 (0.48)
	IBS-only	0.33 (0.42)	0.37 (0.59)	0.04 (0.54)
	Group effect	.002	.002	*ns*

Note. IBS + PMS + DYS ($n = 38$); IBS + PMS ($n = 59$); IBS + DYS ($n = 15$); IBS-only ($n = 114$).

ns: $p > .20$.

*Significant differences ($p < .05$) between IBS-only and other groups.

tom diaries, Heitkemper, Shaver, and Mitchell (1988), in an early study, found higher levels of GI symptoms (e.g., stomach pain) across the menstrual cycle in women with dysmenorrhea as compared to women without dysmenorrhea. No effort was made in that earlier study, however, to identify those who also reported PMS or IBS. In a more recent comparison study of pain sensitivity in women with and without dysmenorrhea, Bajaj et al. (2002) hypothesized that increased sensory perception in patients with dysmenorrhea at menses was related to the activation of afferent nerve fibers induced by inflammatory mediators such as prostaglandins. Activation of silent afferent fibers, which innervate abdominal visceral and somatic organs, could account for the increase in somatic (e.g., backache) and visceral (e.g., abdominal pain) complaints that co-occur with painful uterine cramping pain. Silent afferents are fibers that do not respond to sensory stimulation, but can become activated in the presence of sensitizing factors including ischemia or inflammation (Bajaj et al.).

TABLE 3

Effects of Group on Symptom Checklist-90 Revised Global Severity Index (GSI-90R), Depression, and Anxiety Subscales

	IBS + PMS + DYS, Mean (*SD*)	IBS + PMS, Mean (*SD*)	IBS + DYS, Mean (*SD*)	IBS-Only	Group Effect, *F* (*p* value)
GSI-90R	0.77 (0.49)*	0.83 (0.52)*	0.69 (0.62)	0.47 (0.29)	24.4 (<.001)
Depression	1.05 (0.71)*	1.15 (0.80)*	0.88 (0.74)	0.65 (0.44)	19.3 (<.001)
Anxiety	0.78 (0.77)*	0.75 (0.62)*	0.67 (0.80)	0.37 (0.34)	16.9 (<.001)

*Significant differences ($p < .05$) between IBS-only and IBS + PMS and IBS + PMS + DYS.

In the current study, women in the IBS + DYS group did report higher average backache and abdominal pain at menses. These increases were not statistically significant, likely at least in part to the relatively small sample of IBS women who reported dysmenorrhea only (7%). When dysmenorrhea along with PMS was reported by women, somatic and visceral complaints were increased, suggesting that other mechanisms (e.g., CNS alterations) are needed to explain heightened sensitivity.

PMS was self-reported by approximately 44% of our sample of women with IBS. This percentage is consistent with that reported by Whitehead et al. (2002). PMS describes a predictable cluster of physical and mood symptoms and cognitive disturbances that occur prior to menses (Johnson, 2004). Moderate symptoms that lead to discomfort are reported in 20–40% of healthy women. An additional 3–8% of women experience symptoms severe enough to significantly interfere with daily functioning. This condition is referred to as premenstrual dysphoric disorder (PMDD).

No attempt was made in the current study to determine which of the women who reported PMS qualified for a diagnosis of PMDD. A limited number of studies have examined pain sensitivity in women with PMS and/or PMDD. In a study of 27 women with PMDD and 27 healthy controls, Straneva et al. (2002) noted that women with PMDD had shorter pain time to threshold and tolerance and greater pain unpleasantness ratings during the pain trial. In addition, these women also had lower β-endorphin levels in their luteal phase as compared to healthy controls.

The additive effect of PMS to symptoms experienced by women with IBS suggests several possible explanations. First, women with IBS + PMS are more likely to report more intense or frequent symptoms in general. This finding is supported in part by an earlier report in which we noted women with IBS who report "severe" IBS symptoms were more likely to report menstrual, psychological distress, and somatic symptoms as compared to women with "mild-to-moderate" IBS symptoms. Second, IBS women with PMS, with or without dysmenorrhea, also reported higher levels of psychological distress as compared to those with IBS-alone. Secondary to psychological distress, women in these groups may have been more prone to reporting multiple symptoms of greater severity. The converse may also be true. That is, women who experience more than one painful condition may have more distress secondary to living with chronic (albeit cyclic) pain. It remains to be determined whether physiological differences separate these groups of women.

Limitations

A limitation of the current study was the use of single item to denote dysmenorrhea and two items for PMS; however, the percentages of women classified as dysmenorrheic and/or having PMS were similar to that noted by others. In an earlier study in which diary as well as retrospective questionnaires was used, we noted that women tend to overreport menstrual cramping pain on history (Heitkemper et al., 1988). The use of the daily diary however confirmed that all four symptomatic groups had marked elevations in uterine cramping pain at menses with those categorized as dysmenorrheic reporting the greatest severity of pain (see Figure 1). The fact that those in the IBS + PMS group also tended to report higher daily scores on items related to depression, anxiety, and anger also supports the categorization of women with PMS.

Implications for Practice and Research

Nurses working in primary care, gynecology, and gastroenterology clinics are often at the forefront of managing women with a diagnosis with IBS. A thorough history that includes gynecologic conditions such as PMS and dysmenorrhea is an important first step in the assessment of women with IBS. Clinically, the use of a daily symptom diary for one to two menstrual cycles may help women appreciate the relation between their menstrual cycle as well as cycle-related conditions and their IBS symptoms. For example, noting that bloating increases during the late luteal phase and menses as compared to other cycle phases may reduce anxiety. The use of drugs or herbal therapies for these conditions should also be evaluated.

Treatment of one condition (e.g., PMS) may exacerbate another condition (e.g., IBS). Additional studies that focus on the efficacy of nondrug therapies such as cognitive behavioral therapy on both IBS and gynecologic symptoms are needed.

The results of this study necessitate researchers studying women with IBS also concentrate on the coexistence of common gynecologic conditions. It may be that IBS, PMS, and dysmenorrhea represent components of a multisystemic ill-

ness that also includes somatic symptoms and fatigue. If so, a common pathophysiologic alteration may be at work.

Conclusion

The presence of multiple symptoms in women with IBS challenges healthcare providers to consider multicomponent therapies to alleviate symptom distress. Researchers testing therapeutics in women with IBS need to consider the impact of these common comorbid conditions when symptom severity or intensity is the primary study outcome.

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