ORIGINAL ARTICLE

The Effect of Breathing, Movement, and Meditation on Psychological and Physical Symptoms and Inflammatory Biomarkers in Inflammatory Bowel Disease: A Randomized Controlled Trial

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Background: This study evaluated the effects of the Breath–Body–Mind Workshop (BBMW) (breathing, movement, and meditation) on psychological and physical symptoms and inflammatory biomarkers in inflammatory bowel disease (IBD).

Methods: Twenty-nine IBD patients from the Jill Roberts IBD Center were randomized to BBMW or an educational seminar. Beck Anxiety Inventory, Beck Depression Inventory, Brief Symptom Inventory 18, IBD Questionnaire, Perceived Disability Scale, Perceived Stress Questionnaire, Digestive Disease Acceptance Questionnaire, Brief Illness Perception Questionnaire, fecal calprotectin, C-reactive protein, and physiological measures were obtained at baseline and weeks 6 and 26.

Results: The BBMW group significantly improved between baseline and week 6 on Brief Symptom Inventory 18 ($P = 0.02$), Beck Anxiety Inventory ($P = 0.02$), and IBD Questionnaire ($P = 0.01$) and between baseline and week 26 on Brief Symptom Inventory 18 ($P = 0.04$), Beck Anxiety Inventory ($P = 0.03$), Beck Depression Inventory ($P = 0.01$), IBD Questionnaire ($P = 0.01$), Perceived Disability Scale ($P = 0.001$), and Perceived Stress Questionnaire ($P = 0.01$) by paired t tests. No significant changes occurred in the educational seminar group at week 6 or 26. By week 26, median C-reactive protein values decreased significantly in the BBMW group ($P = 0.01$ by Wilcoxon signed-rank test) versus no significant change in the educational seminar group.

Conclusions: In patients with IBD, participation in the BBMW was associated with significant improvements in psychological and physical symptoms, quality of life, and C-reactive protein. Mind–body interventions, such as BBMW, which emphasize Voluntarily Regulated Breathing Practices, may have significant long-lasting benefits for IBD symptoms, anxiety, depression, quality of life, and inflammation. BBMW, a promising adjunctive treatment for IBD, warrants further study.

Inflammatory bowel disease (IBD) is a chronic lifelong illness characterized by recurrences and remissions that affect physical and psychological well-being and incur substantial health care costs.[1] IBD is a dysregulated immune-mediated inflammatory response to environmental factors.[2,3] Despite recent advances in optimizing treatment for IBD with biological and immunomodulating therapies, many patients do not achieve remission and may experience medical treatment-related adverse events or significant disease-related morbidity and mortality.[4,5] Conventional treatments for IBD focus on ameliorating symptoms and inflammation through pharmacological interventions and patient education to enhance medication adherence.

When conventional treatments fall short of disease remission, patients may turn to complementary and alternative medicine. Up to 60% of patients with IBD currently use or previously used complementary and alternative medicine for better control of their disease or to ameliorate side effects of conventional therapy.[6,7] Health care providers, conscious of the limitations, costs, and adverse effects of conventional treatments for IBD, are also seeking safer alternative approaches.[8] However, there is limited high-quality evidence regarding the effects of specific forms of complementary and alternative medicine on symptoms of IBD and inflammatory markers.

Mind–body approaches, particularly Voluntarily Regulated Breathing Practices (VRBPs), have been hypothesized to affect mechanisms involved in the pathogenesis of IBD, including the autonomic nervous system, inflammation, and the hypothalamic–pituitary–adrenal axis.[9–15] Mind–body practices can reduce symptoms of stress and anxiety, particularly when they are associated with noxious physical experiences.[11–13] Symptoms of anxiety and depression have been estimated at 60% to 80% during IBD flares and 35% during remissions.[7,14] Psychological distress affects both quality of life and severity of IBD symptoms. Therefore, interventions that alleviate psychological distress should also reduce IBD symptoms. Synergistically, slow VRBPs reduce sympathetic overactivity, increase parasympathetic underactivity, and thereby trigger anti-inflammatory cascades potentially reducing inflammation. The use of these mind–body practices would cause very few side effects[9,12] and could reduce side effects and mounting costs of medications used to treat IBD.

The importance of activating the body's innate healing mechanisms, in addition to symptom suppression, has not been adequately appreciated. Breath–Body–Mind Workshop (BBMW), a program of movement, VRBPs, and meditation, was chosen because it includes practices that have been shown to be effective in reducing perceived stress, anxiety, depression, posttraumatic stress, inflammation, and pain.[9,11–13,15–19]

The purpose of this study was to evaluate the effects of a mind–body intervention called the BBMW, as an adjunct to standard pharmacotherapy in patients with mild-to-moderate IBD, on physical and psychological symptoms, quality of life, and inflammatory biomarkers. We hypothesized that psychological distress, IBD symptomatology, and inflammatory biomarkers would improve in response to the BBMW compared with an educational intervention.

MATERIALS AND METHODS

Participants

Twenty-nine patients with IBD (aged 18–85 yr) were recruited from the Jill Roberts Center for IBD in New York at the time of their outpatient clinic visit, by telephone interview, or through flyers. Flyers were also placed in the collaborating IBD center at Columbia University.

Randomization

After signing informed consent, subjects were randomized to the 2 groups according to numbers assigned to each subject as they arrived at the first session (baseline visit). Each subject was designated a number (001, 002, 003, etc.) in the order of his or her arrival. Those subjects with odd numbers were assigned to the study group; those with even numbers were assigned to the control group (Fig. 1).

Measures

Demographic Variables

Data were collected, including age, ethnicity, gender, allergies, medications, medical history, surgical history, smoking history, and family history of IBD, at week 0 to assess epidemiological factors.

Psychological Measures, IBD Symptoms, and Quality of Life

The first objective of this study was to determine how participation in BBMW would affect psychological measures (indices of anxiety, depression, and perceived stress), IBD symptoms, and quality of life in comparison with educational seminar (ES) patients with IBD. Both groups had the following instruments administered before, during, and after their respective programs at weeks 0, 6, and 26.

Brief Symptom Inventory 18. The Brief Symptom Inventory 18 (BSI-18) is an 18-item measure of psychological distress over the previous 7 days. Each item is rated on a 5-point (0–4) Likert-type scale, where 0 is "not at all" and 4 is "extremely." The BSI-18 assesses somatization, depression, and anxiety, symptom intensity, and total number of symptoms. Total scores range from 0 to 72 with higher scores indicating greater levels of distress.[20]

Beck Anxiety Inventory. The Beck Anxiety Inventory (BAI) is a 21-item anxiety symptom inventory. Some examples of symptoms include "wobbliness in legs," "scared," and "fear of losing control." Patients are asked the degree to which each symptom bothered them in the previous week. Each item is scored on a 4-point scale, where 0 is not at all and 3 is "could barely stand it." Scores range from 0 to 63. Anxiety scores
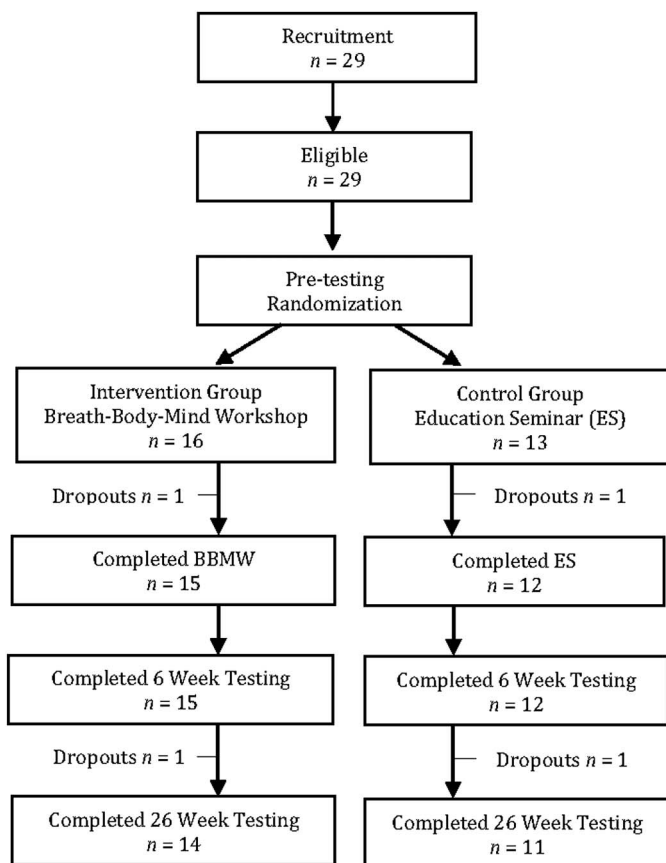
FIGURE 1. Study flow chart.

correspond to the following severity levels: 0 to 9 minimal, 10 to 16 mild, 17 to 29 moderate, and 30 to 63 severe.[21]

Beck Depression Inventory. The Beck Depression Inventory (BDI) is a 21-item self-report inventory that assesses depression. Items are scored on a 4-point scale from 0 to 3. Total scores range from 0 to 63 with higher scores reflecting a more depressed mood. Depression severity score ranges are 0 to 13 minimal, 14 to 19 mild, 20 to 28 moderate, and 29 to 63 severe. A score greater than 11 is suggestive of clinical depression in the general population.[22]

IBD Questionnaire. The IBD Questionnaire (IBDQ) is a 32-item questionnaire designed to measure the effects of IBD on daily function and quality of life in IBD patients. The questions address 4 dimensions: bowel symptoms (10 items), systemic symptoms (5 items), emotional function (12 items), and social function (5 items). Each item is scored on a 7-point scale, from 1 (worst situation) to 7 (best situation). Total scores range from 32 to 224 with higher scores indicating better health-related quality of life.[23]

Perceived Disability Scale. The Perceived Disability Scale (PDS) is a 10-item instrument that assesses the degree to which patients feel limited by their condition, in this case, by their IBD,

across 10 domains: home responsibilities, occupation/education, recreation, social, sexual, physical, cognitive, sleep, self-care, and basic life functions. Each item is scored on a scale from 0 "no disability" to 10 "total disability." Total scores range from 0 to 100. Higher scores represent greater perceived disability.[24] In a previous study of 71 adults (mean age 37.4 yr, range 21–69 yr; 59% women) with IBD documented by colonoscopy, the PDS demonstrated excellent internal consistency (Cronbach's alpha = 0.92). The PDS demonstrated good concurrent validity with IBDQ total score, indicating that the PDS is a reliable and valid measure of perceived disability in IBD.[25]

Perceived Stress Questionnaire. The Perceived Stress Questionnaire (PSQ) is a 30-item assessment tool designed to measure 7 dimensions of stress: harassment, irritability, lack of joy, fatigue, worries, tension, and overload. Each item is scored on a 4-point scale, where 1 is "almost never" and 4 is "usually." Total scores range from 30 to 120.[26]

Digestive Disease Acceptance Questionnaire. The Digestive Disease Acceptance Questionnaire (DDAQ) has 20 items asking about symptom tolerance and active behavioral engagement in daily life activities despite digestive symptoms. Each item is rated on a 7-point Likert scale ranging from 0 "never true" to 6 "always true." The total score range is 0 to 120 with higher scores indicating greater disease acceptance.[24]

Brief Illness Perception Questionnaire. The Brief Illness Perception Questionnaire (BIPQ) has 9 items, 8 of which are rated on a 0 to 10 Likert scale ranging, e.g., from 0 "no effect at all" to 10 "severely affects my life," with total scores ranging from 0 to 80. Items assess cognitive and emotional illness representations and illness comprehensibility. One open-ended question asks patients to list the 3 most important causal factors in their illness.[27]

Inflammatory Biomarkers

To assess effects of participation in BBMW on inflammatory biomarkers, stool fecal calprotectin (FCP) and serum C-reactive protein (CRP) were measured at 0, 6, and 26 weeks. FCP has been used as a marker of neutrophilic intestinal inflammation.[28] Calprotectin is an abundant calcium-binding protein derived primarily from neutrophils and monocytes and reactive macrophages, to a lesser extent. Calprotectin is found in stool and plasma and can be markedly elevated in infectious and inflammatory conditions, such as IBD and rheumatoid disease. CRP is produced almost exclusively in the liver by hepatocytes in response to stimulation by proinflammatory cytokines, such as interleukin 6, tumor necrosis factor α, and interleukin 1-β. CRP is an acute-phase reactant with a short half-life. Thus, it is well suited as a marker of disease activity in IBD.[29]

Physiological Measures

To determine how participation in BBMW would affect physiological measures in patients with IBD, body temperature, blood pressure, and pulse were measured at 0, 6, and 26 weeks.

Interventions

BBMW Study Group

The 9-hour BBMW was administered on 2 consecutive days with 6 hours on the first day and 3 hours on the second day. During this workshop, subjects were taught 4 breathing techniques, Qigong movements coordinated with breathing, and Open Focus meditation (for workshop schedule, see Appendix, Supplemental Digital Content 1, http://links.lww.com/IBD/B121).

Dr. R. P. B. administered the BBMW and conducted all BBMW follow-up sessions. Dr. R. P. B. developed the BBMW based on his experience studying martial arts, aikido, zen, yoga, and Qigong over the past 50 years. He is a certified instructor of aikido (fourth Dan), yoga, Qigong, and Open Focus Attention Training. He had no involvement in testing or data analysis in this study.

Each session began with a movement sequence called *The Four Golden Wheels* from Qigong Master Robert Peng.[30] Qigong movements, believed to circulate and balance energy, have shown benefits in stress, anxiety, depression, well-being, and inflammation.[31–34]

The core breath technique, coherent breathing, is paced at 5 breaths per minute (bpm) with equal inhalation and exhalation using a chime tone. For most adults, optimal sympathovagal balance is attained with coherent breathing (or resonance breathing) at a rate between 4.5 and 6 bpm. Resistance breathing (creating resistance to airflow by a slight contraction of the laryngeal muscles) augments the calming effects of coherent breathing. The breathing practice is further enhanced by breath moving, the imaginative moving of the breath in circuits throughout the body, derived from prayer practices of Russian Orthodox monks and from Qigong.[9,15] "Ha" breath, a brief activating practice, entails moderately forceful inhalation and forceful exhalation while shouting "Ha" with arm movements, at a rate of 15 bpm.[15] The sequence used comprisedof 3 rounds of 15 "Ha" breaths with 15 seconds rest after each round.

Open Focus Attention Training was developed by Les Fehmi.[35–37] By teaching subjects to shift between narrow and open attention modes and to focus their attention on internal and external space, Open Focus Attention Training has been used to relieve pain and alter the perception of pain.

BBMW participants were given a 30-minute CD recording of a chime tone to pace their breathing at 5 bpm during at-home practice of the mind–body techniques taught in the workshop. They were encouraged to do 20 minutes per day of coherent breathing with resistance and breath moving followed by 3 minutes supine rest. Each study group participant was instructed to keep a daily practice log. Weekly follow-up sessions of 90 minutes each were offered for 6 weeks and then monthly from week 7 through week 26.

ES Active Control

The ES was taught by the faculty and staff of the Jill Roberts Center for Inflammatory Bowel Disease, New York Presbyterian Hospital, Weil Cornell Medical Center: E. J. Scherl, Director, Jill Roberts Center; Brian Bosworth, Program Director, Gastroenterology Fellowship; and Vinita Jacob, Director Interdisciplinary Education Division of Gastroenterology and Hepatology. At the start of the study, the active control group participated in a weekend ES that included one 6-hour day followed by two 90-minute sessions (total 9 h) during which they received information about IBD and its treatment. During weeks 1 to 6, subjects participated in weekly educational lectures held at the Jill Roberts IBD Center. The weekly educational lectures encompassed the following topics: importance of medication compliance, impact of IBD on fertility and pregnancy, effect of disease and surgery on sex drive and cosmetic perception, impact of daily stress and depression on quality of life in IBD, and the importance of nutrition in IBD. At the end of the 26-week study, control group subjects were offered the opportunity to participate in a 2-day BBMW.

An active control group was deemed preferable to a waitlist control to reduce the possible effects of patient expectations, time with the study staff, and group interactions. The amount of time given to each intervention—BBMW and the ES—was the same.

Statistical Analyses

Descriptive statistics (including mean, SD, median, range) for the questionnaire measures were calculated for BBMW and ES groups, separately at baseline, 6 weeks, and 26 weeks. The paired *t* test was used to calculate change in the questionnaire measures from baseline to 6 weeks and from baseline to 26 weeks in the BBMW group and education group separately (i.e., within-group analysis). The Wilcoxon signed-rank test was used to measure changes in CRP between baseline and 6 weeks and between baseline and 26 weeks for each group separately. The Wilcoxon signed-rank test was used to compare median change in CRP and FCP (with "change" defined as 6-week score minus baseline score and 26-week score minus baseline score) between the BBMW group and the ES group (i.e., between-group analysis). All *P* values are 2 sided with statistical significance evaluated at the 0.05 alpha level. *P* values were not corrected for multiple comparisons or multiplicity of outcomes given the exploratory (i.e., hypothesis generating) nature of this pilot study. All analyses were performed in SPSS Version 21.0 (SPSS Inc., Chicago, IL).

ETHICAL CONSIDERATIONS

The institutional review boards at both Weill Cornell Medical Center and Columbia University Medical Center approved this study.

RESULTS

Subject Characteristics: Demographic Data, Medical History, and Baseline Measures

Patient characteristics, including demographics, medications, medical history, and surgical history, are shown in Table 1. The

TABLE 1. Subject Demographics, Medications, Medical History, and Surgical History

Subject No.	Sex	Age, yr	Smoking History	Pack, yr	Medications	GI Surgical History	Disease Type	Disease Duration, yr
BBMW study group								
1	M	49	N	NA	Humira	Small bowel resection; ostomy; resize ostomy and resection; removal anus/colon	IC	30
3	F	36	N	NA	Asacol	N	CD	1
5	M	68	Y (past)	55	Azathioprine	N	UC	4
7	F	59	N	NA	Nexium, Bactrim	Small bowel resection	CD	4–5
9	F	44	Y (past)	15	Apriso; Entocort; Xifaxan; Vitamin D	Appendectomy	CD	1
11	M	39	N	NA	Apriso, Canasa, Cortifoam	Perianal fistula drainage	CD	19
13	F	41	Y (past)	5	Colazal, Canasa	N	UC	23
15	M	33	Y	3	Apriso, Remicade	N	CD	9
17	M	73	Y (past)	5	Humira	Hernia 2×	LP	7
19	M	31	Y (past)	5	Remicade; Pentasa; Apriso	N	CD	<1
21	M	60	Y (past)	15	Remicade	Resection; mitral valve repair; resection and repair rectal prolapse	CD	33
23	F	35	Y (past)	5	Apriso; Remicade	N	UC	3
25	F	55	N	NA	Circumen	Fissure/fistula repairs; subtotal colectomy; ileostomy reversal; stricture repair	CD	12
27	M	45	N	NA	Prednisone	Bowel resection; bowel resection	CD	25
29	F	71	N	NA	Vitamin D; B12	Small benign renal tumor	CD	4
ES control group								
2	M	61	N	NA	Pentasa; Opium tincture; VSL no. 3; Vitamin D	Total proctocolectomy	UC	44
4	F	67	Y (past)	17	None	N	UC	22
6	F	60	N	NA	Apriso	N	UC	1
8	F	74	N	NA	None	N	UC	4
10	M	70	N	NA	Pentasa; Cipro; Metronidazole; Vitamin D3	Partial colectomy; revision of anastomosis	CD	49
12	M	85	Y (past)	15	Budesonide	Renal stent	CD	51
14	F	43	N	NA	Apriso	N	CD	10
16	M	66	N	NA	Apriso, Probiotics	N	CD	15
18	F	76	N	NA	Asacol	N	CD	6
20	F	42	Y (past)	1.25	None	N	UC	10
22	F	46	Y (past)	17	Apriso; Canasa	N	UC	12
24	F	57	Y (past)	22.5	Remicade	N	CD	1
26	F	25	N	NA	Apriso, Cimzia, Entocort	G tube; short bowel resection	CD	15
28	F	48	N	NA	Cimzia	Ileostomy; ileostomy correction; anovaginal fistula repair	CD	12

CD, Crohn's disease; F, female; IC, indeterminate colitis; LP, lymphocytic pancolitis; M, male; N, no; NA, not applicable; UC, ulcerative colitis; Y, yes.

subjects were 29 adults (12 men and 17 women) between 25 and 85 years of age, mean age 54 years. All but 5 subjects were on maintenance medications, including corticosteroids, thiopurines, antitumor necrosis factor therapies, and others. Twelve had a history of gastrointestinal (GI) surgery and 2 of renal surgery. Diagnoses included ulcerative colitis (n = 9), Crohn's disease (n = 18), indeterminate colitis (n = 1), and lymphocytic pancolitis (n = 1). The duration of illness ranged from less than 1 to 55 years (Table 1).

There were no statistically significant differences in demographic characteristics between the BBMW group and the ES group (Table 2). Although the BBMW group was 53% men versus the ES group 28% men, this difference did not reach significance (P = 0.18). The mean age of the ES group was 9.3 years higher than the BBMW group. This approached but did not reach statistical significance (P = 0.11).

Of note, mean baseline BSI-18 and BIPQ were significantly higher in BBMW group compared with the ES group (P = 0.02 and P = 0.02, respectively, by paired t test). Mean baseline IBDQ showed a lower nonsignificant trend in BBMW group compared with ES (P = 0.09 by paired t test). Mean PDS and mean PSQ were nonsignificantly higher (P = 0.37 and P = 0.35, respectively, by paired t test) in BBMW group compared with ES at baseline.

Baseline median CRP was nonsignificantly lower in BBMW group compared with ES, with 1026.0 versus 8590.0, respectively (P = 0.09 by Wilcoxon signed-rank test for comparison of median values) (Table 2).

One adverse reaction occurred in the control group: one patient reported that the educational sessions added to her distress and anxiety and she subsequently stopped attending. No adverse reactions were observed in the BBMW group.

Effects on Anxiety, Depression, IBD Symptoms, and Quality of Life Indices

Although BSI-18 baseline values were higher in the BBMW than ES group, both fell within the lowest quartile (BSI-18 range, 0–72), reflected a modest level of distress, and were comparable with mean scores (9.8 ± 10.6) in the study of psychological adjustment to IBD in 38 adults by Kiebles et al.[24] Baseline mean BAI for the BBMW group (12.13 ± 7.49) was within mild range (10–16) and for the ES group (7.92 ± 4.01) within minimal range (0–9), suggesting a greater level of distress in the former. Mean baseline BDI scores for both groups, BBMW (4.20 ± 4.00) and ES (3.83 ± 2.72), were within the minimal range (0–13). IBDQ mean baseline scores for BBMW (146.43 ± 31.06) and ES (164.18 ± 18.95) were similar to mean scores (165.7 ± 33.2) reported by Kiebles et al[24] and registered in the middle of the range (0–224). The mean baseline PDS scores for BBMW (24.47 ± 17.60) and ES (19.09 ± 12.19) were in the middle of the range (0–100) and were consistent with scores reported by Kiebles et al (2010) for adults experiencing a flare in IBD (mean PDS = 20.45 ± 23.4). For both the BBMW

TABLE 2. BBMW Versus ES: Comparison of Baseline Characteristics and Mean Baseline Scores

	BBMW	ES	Significance P^a
Male/female	8/7 (53.3% male)	4/10 (28.6% male)	0.18
Mean age (yr)	49.27 ± 14.21	58.57 ± 16.22	0.11

Tests	Baseline Scores ± SD	Baseline Scores ± SD	P
BSI-18	15.80 ± 10.71[15]	8.42 ± 4.06[12]	0.02[a]
BAI	12.13 ± 7.49[15]	7.92 ± 4.01[12]	0.08
BDI	4.20 ± 4.00[15]	3.83 ± 2.72[12]	0.78
IBDQ	146.43 ± 31.06[14]	164.18 ± 18.95[11]	0.09
PDS	24.47 ± 17.60[15]	19.09 ± 12.19[11]	0.37
PSQ	72.40 ± 13.62[15]	66.83 ± 15.90[12]	0.35
DDAQ	70.14 ± 7.78[14]	66.17 ± 10.56[12]	0.29
BIPQ	50.50 ± 9.40[14]	41.33 ± 8.34[12]	0.02[a]

	Breath-Body-Mind			ES			
Inflammatory Markers	Median	Min	Max	Median	Min	Max	Significance P^b
CRP (ng/mL)	1026.0[15]	123.8	17,480.0	8590.0[12]	169.42	26,200.0	0.09
FCP (μg/g)	216.3[15]	25.6	4067.7	223.6[11]	27.0	2126.7	0.80

[11], n = 11; [12], n = 12; [13], n = 13; [14], n = 14; [15], n = 15.
[a]Paired t tests for mean comparisons.
[b]Wilcoxon signed-rank test for median comparisons.

TABLE 3. BBMW Group: Significance of Change in Mean Scores

Tests	Baseline Scores ± SD	Week 6 Scores ± SD	Week 6, *P*	Baseline Scores ± SD	Week 26 Scores ± SD	Week 26, *P*[a]
BSI-18	15.80 ± 10.71[15]	11.00 ± 6.51[15]	0.02[a]	16.00 ± 11.09[14]	9.64 ± 6.87[14]	0.04[a]
BAI	12.13 ± 7.49[15]	10.07 ± 8.36[15]	0.02[a]	11.93 ± 7.73[14]	9.29 ± 7.56[14]	0.03[a]
BDI	4.20 ± 4.00[15]	3.80 ± 4.00[15]	0.14	4.21 ± 4.15[14]	3.00 ± 3.76[14]	0.01[a]
IBDQ	146.43 ± 31.06[14]	159.00 ± 28.16[14]	0.01[a]	146.62 ± 32.32[13]	173.46 ± 24.70[13]	0.01[a]
PDS	24.47 ± 17.60[15]	21.33 ± 15.96[15]	0.23	23.571 ± 17.91[14]	16.78 ± 16.79[14]	0.001[a]
PSQ	71.31 ± 14.26[13]	70.46 ± 13.49[13]	0.71	73.71 ± 13.11[14]	62.36 ± 15.98[14]	0.01[a]
DDAQ	70.14 ± 7.78[14]	74.07 ± 16.46[14]	0.34	69.92 ± 8.06[13]	72.08 ± 8.50[13]	0.46
BIPQ	50.50 ± 9.4034[14]	50.79 ± 10.04[14]	0.90	49.69 ± 9.27[13]	45.23 ± 11.01[13]	0.17

[8], n = 8; [10], n = 10; [11], n = 11; [12], n = 12; [13], n = 13; [14], n = 14; [15], n = 15.
[a]Statistically significant by paired *t* test.

(72.40 ± 13.62) and ES groups (66.83 ± 15.90), mean PSQ scores were in the high middle range (0–100) and were similar to scores found by Kiebles et al[24] (69.3 ± 16.7).

Within-group comparisons indicated that between baseline and week 6, the BBMW group showed statistically significant improvements in IBD symptoms on BSI-18 (*P* = 0.02), anxiety (BAI, *P* = 0.02), and quality of life (IBDQ, *P* = 0.01) (Table 3). Between baseline and week 26, the BBMW group continued to show statistically significant improvements in BSI-18 (*P* = 0.04), BAI (*P* = 0.03), and IBDQ (*P* = 0.01). Furthermore, there were significant improvements in social function (PDS, *P* = 0.001), perceived stress (PSQ, *P* = 0.01), and depression (BDI, *P* = 0.01) (Table 3). In contrast, the ES group showed no significant changes in BSI-18, BAI, BDI, IBDQ, PDS, or PSQ scores at 6 or 26 weeks (Table 4).

Two of the 8 psychological measures, the DDAQ and BIPQ, did not show significant changes in either group at 6 or 26 weeks (Tables 3 and 4).

Intergroup comparison of the mean change in scores at week 6 showed that on BSI-18, the BBMW group had a statistically

significant greater improvement (−4.80 ± 6.78) compared with ES (0.91 ± 5.23) (*P* = 0.02) (Table 5). Also, at week 6, improvement on IBDQ was greater in the BBMW group (12.57 ± 15.85) compared with the ES group (−1.73 ± 19.95) (*P* = 0.08), although it did not reach statistical significance (Table 5). By week 26, in comparison with the ES group, the BBMW group showed statistically significant greater improvements in BSI-18 (*P* = 0.01), IBDQ (*P* = 0.04), PDS (*P* = 0.05), and PSQ (*P* = 0.01) with nonsignificant trend toward greater improvements in BAI (*P* = 0.11) and BDI (*P* = 0.27) (Table 6).

Effects on Inflammatory Biomarkers

At week 26, median CRP values showed significant improvement in the BBMW group compared with baseline (730.0 versus 836.0 ng/mL, respectively, *P* = 0.01). In contrast, no significant change occurred in CRP in the ES group (*P* = 0.39) (Table 7).

Although not statistically significant, there was a trend toward lower median FCP in the BBMW group at week 6 compared with baseline (149.9 versus 216.3 μg/g, respectively,

TABLE 4. ES Group: Significance of Change in Mean Scores

Tests	Baseline Scores ± SD	Week 6 Scores ± SD	Week 6, *P*	Baseline Scores ± SD	Week 26 Scores ± SD	Week 26, *P*[a]
BSI-18	8.42 ± 4.06[12]	9.33 ± 7.56[12]	0.56	8.55 ± 4.23[11]	10.91 ± 9.06[11]	0.30
BAI	7.92 ± 4.01[12]	6.33 ± 4.68[12]	0.22	7.64 ± 4.08[11]	7.64 ± 5.45[11]	1.00
BDI	3.55 ± 2.66[11]	2.82 ± 1.72[11]	0.23	3.82 ± 2.86[11]	3.46 ± 3.05[11]	0.59
IBDQ	164.18 ± 18.95[11]	162.46 ± 24.87[11]	0.78	164.50 ± 22.62[8]	164.38 ± 38.03[8]	0.99
PDS	19.09 ± 12.19[11]	20.82 ± 12.40[11]	0.65	17.50 ± 11.59[10]	19.30 ± 17.86[10]	0.66
PSQ	66.83 ± 15.90[12]	68.50 ± 16.41[12]	0.38	67.09 ± 16.65[11]	70.36 ± 21.34[11]	0.29
DDAQ	66.17 ± 10.56[12]	65.67 ± 5.18[12]	0.88	66.46 ± 11.02[11]	66.72 ± 12.88[11]	0.93
BIPQ	41.3 ± 8.34[12]	42.00 ± 6.80[12]	0.78	41.91 ± 8.49[11]	40.00 ± 10.89[11]	0.56

[8], n = 8; [10], n = 10; [11], n = 11; [12], n = 12; [13], n = 13; [14], n = 14; [15], n = 15.
[a]Statistically significant by paired *t* test.

TABLE 5. BBMW Versus ES: Comparison of Mean Changes in Scores: Baseline to 6 Weeks

Tests	BBMW Group Change ± SD	ES Group Change ± SD	Significance P^a
BSI-18	−4.80 ± 6.78[15]	0.91 ± 5.23[12]	0.02[a]
BAI	−2.07 ± 3.17[15]	−1.58 ± 4.23[12]	0.75
BDI	−0.40 ± 0.99[15]	−0.72 ± 1.90[11]	0.61
IBDQ	12.57 ± 15.85[14]	−1.73 ± 19.91[11]	0.08
PDS	−3.13 ± 9.66[15]	1.72 ± 12.15[11]	0.29
PSQ	−0.85 ± 8.12[13]	1.67 ± 6.33[12]	0.40
DDAQ	3.93 ± 14.96[14]	−0.50 ± 11.41[12]	0.40
BIPQ	0.29 ± 8.04[14]	0.67 ± 8.19[12]	0.91

[8], n = 8; [10], n = 10; [11], n = 11; [12], n = 12; [13], n = 13; [14], n = 14; [15], n = 15.
[a]Statistically significant by paired *t* test.

$P = 0.11$). This trend did not continue in the BBMW at week 26 compared with baseline. In the ES control group, a trend that did not reach statistical significance was noted in median FCP, which was lower at 6 weeks compared with baseline ($P = 0.09$). No significant changes were found in FCP at week 26 in either group (Table 8).

Effects on Physiologic Measures

At 6 weeks, there was a statistically significant increase in mean temperature in the BBMW group compared with baseline (98.8 ± 0.4 versus 97.8 ± 0.8°F, respectively, $P = 0.02$) with no significant changes in systolic blood pressure ($P = 0.68$), diastolic blood pressure ($P = 0.67$), or pulse ($P = 0.10$). At 26 weeks, there were no significant changes in any of these measures compared with baseline in the BBMW group. Neither at 6 weeks nor at 26 weeks were there any significant changes in vital signs in the ES group.

TABLE 6. BBMW Versus ES: Comparison of Mean Changes in Scores: Baseline to 26 Weeks

Tests	BBMW Group Change ± SD	ES Group Change ± SD	Significance P^a
BSI-18	−6.36 ± 6.77[14]	2.36 ± 7.12[11]	0.01[a]
BAI	−2.64 ± 4.18[14]	0.00 ± 3.79[11]	0.11
BDI	−1.21 ± 1.37[14]	−0.36 ± 2.16[11]	0.27
IBDQ	26.85 ± 29.11[13]	−0.13 ± 25.35[8]	0.04[a]
PDS	−7.50 ± 6.94[14]	1.80 ± 12.56[10]	0.05[a]
PSQ	−11.36 ± 14.78[14]	3.27 ± 9.77[11]	0.01[a]
DDAQ	2.15 ± 10.25[13]	0.27 ± 10.25[11]	0.66
BIPQ	−4.46 ± 11.00[13]	−1.90 ± 10.45[11]	0.57

[8], n = 8; [10], n = 10; [11], n = 11; [12], n = 12; [13], n = 13; [14], n = 14; [15], n = 15.
[a]Statistically significant by paired *t* test.

TABLE 7. Comparison of CRP Median Values

Group	Baseline (ng/mL)	Week 6 (ng/mL)	Week 6, P^a	Baseline (ng/mL)	Week 26 (ng/mL)	Week 26, P^a
BBMW	1026.0[15]	2560.0[15]	0.40	836.0[9]	730.0[9]	0.01[a]
ES	8590.0[12]	6570.0[12]	1.00	9240.0[10]	7180.0[10]	0.39

[9], n = 9; [10], n = 10; [12], n = 12; [14], n = 14; [15], n = 15.
[a]Statistically significant by Wilcoxon signed-rank test for median comparisons.

DISCUSSION

After participation in the BBMW, patients had significantly decreased physical symptoms and anxiety with improved quality of life, between baseline and week 6. By week 26, the BBMW group showed significant improvements in anxiety, stress, depression, physical symptoms, quality of life, and social function compared with baseline (Table 3). Furthermore, one of the inflammatory markers, CRP, was significantly reduced at week 26, suggesting that the BBMW intervention may have reduced inflammation. In contrast, the ES group showed no significant changes in psychological indices, physical symptoms, or inflammatory markers at the 26-week mark compared with baseline. Comparison between the 2 groups showed significant advantages for the BBMW over the ES control at week 26 for changes in psychological and physical symptoms (BSI-18, $P = 0.01$; IBDQ, $P = 0.04$; PDS, $P = 0.05$; PSQ, $P = 0.01$) and CRP ($P = 0.01$) and a nonsignificant trend for greater improvements in anxiety (BAI, $P = 0.11$) and depression (BDI, $P = 0.27$) (Table 6).

No significant differences were found between the BBMW and ES groups at either 6 or 26 weeks on the DDAQ and BIPQ. These tests have been used in a limited number of studies compared with the other tests. Also, they focus on questions about illness acceptance (DDAQ) and illness representations and comprehensibility (BIPQ), which are more heavily affected by the individual's personality, coping styles, and cognitive functions, in contrast to the other psychological measures described above, wherein questions are aimed more directly at evaluating symptoms. Even on the IBDQ quality of life measure, most of the questions are more directly related to the effects of the symptoms as opposed to how the individual conceptualizes or accepts their illness. It is possible that

TABLE 8. Comparison of FCP Median Values

Group	Baseline (μg/g)	Week 6 (μg/g)	Week 6, P^a	Baseline (μg/g)	Week 26 (μg/g)	Week 26, P^a
BBMW	216.3[15]	149.9[15]	0.11	175.4[14]	155.9[14]	0.78
ES	157.8[10]	78.6[10]	0.09	175.8[10]	341.5[10]	0.59

[9], n = 9; [10], n = 10; [12], n = 12; [14], n = 14; [15], n = 15.
[a]Significance by Wilcoxon signed-rank test for median comparisons.

differences would be found in larger studies that could detect the nuances addressed in the DDAQ and BIPQ.

The mean baseline values used for the paired *t* test for comparison of mean values between weeks 0 and 6 and between weeks 0 and 26 differed because of reductions in the number of subjects (1 dropout from each group). Similarly, the median baseline values used for the Wilcoxon signed-rank test for comparison of median values between weeks 0 and 6 and between weeks 0 and 26 differed because of reductions in the number of subjects completing tests. Only those subjects who completed test measures at both paired time points, 0 and 6 weeks or 0 and 26 weeks, were included in the analysis. The number of subjects (n) with reported test scores varied between 9 and 15, not only between time points but also at the same time point. This occurred because some participants had to travel 2 or 3 hours to get home during severe weather (heavy rain, cold winter weather, snow, and icy conditions). Elderly and ill, they were worried about getting home and therefore left before completing all written test and, in some cases, before giving their blood or stool samples.

The ES group showed a transient significantly lower FCP level at week 6, but not at week 26. The ES, which emphasized the importance of medication and dietary regimens, may have temporarily improved compliance, followed by a return to usual habits and baseline levels of this inflammatory marker.

Disturbances in psychoneuroendocrine–immune modulation may play a central role in the pathogenesis of IBD.[38–41] The autonomic nervous system, particularly the parasympathetic nervous system (PNS), modulates the immune system in chronic inflammatory disease and has antinociceptive effects. Patients with IBD have elevated sympathetic activity and reduced parasympathetic activity, based on heart rate variability.[42,43] Evidence suggests that stress and other negative emotional states may adversely affect the course of IBD by changing GI motility, increasing visceral pain perception, changing GI secretion, increasing intestinal permeability, and negatively affecting GI mucosal regeneration and blood flow.[39] The vagus nerve–mediated anti-inflammatory reflex is essential to prevent and repair GI tissue damage.[41–44]

Evidence supports the concept that coherent breathing (gentle breathing at 5 bpm, with equal inhalation and exhalation) increases activity of the PNS through afferent interoceptive pathways from the respiratory system (mechanoreceptors, chemoreceptors, and baroreceptors) through the vagal nerves.[9,44] The PNS modulates psychoneuroendocrine–immune systems, maintaining homeostasis through afferents (to the hypothalamus, central autonomic nervous system, limbic system, thalamus, and cortex) and efferents (cholinergic anti-inflammatory pathways).[45,46] A recent functional magnetic resonance imaging study of slow-paced breathing at 5.5 bpm (within the coherent breath range) showed increased activity in the dorsal pons, hypothalamus, thalamus, basal ganglia, and sensorimotor cortex.[47] The 5.5-bpm rate attenuated autonomic and cardiovascular responses to challenges, such as hypoxic stress. Coherent breathing may be beneficial in IBD by increasing PNS activity, reducing perceived stress,

alleviating negative psychological states that exacerbate the condition, and enhancing PNS anti-inflammatory effects.

Additional limitations of this study should be noted. The study population is small and heterogeneous. It is not unusual to find some intergroup differences in studies of this size. For example, the gender ratios of the 2 groups differed: the BBMW group was 53% men and the ES group 28% men. Also, the mean age of the BBMW group (49.27 ± 14.21) and of the ES (58.57 ± 16.22) differed by 9.30 years. Neither of these intergroup differences attained statistical significance. However, the extent to which they may be clinically meaningful would have to be determined by a larger study.

Mean baseline BSI-18 was significantly higher in the BBMW group compared with the ES group ($P = 0.02$), suggesting greater distress and symptomatology. The mean IBDQ was lower (nonsignificant trend) in the BBMW group compared with the ES at baseline ($P = 0.09$). This would be consistent in that the group with greater distress and symptomatology would be expected to have a lower quality of life. Despite starting with higher scores on the BSI-18 and lower scores on the IBDQ, the BBMW group achieved significantly greater improvements as compared with the ES control group. Baseline median CRP was nonsignificantly lower in the BBMW group compared with ES group, with 1026.0 versus 8590.0 ng/mL, respectively ($P = 0.09$ by the Wilcoxon signed-rank test for comparison of median values). The relatively lower CRP in the BBMW group would seem to be inconsistent with their comparatively higher BSI-18 and lower IBDQ scores. Though the BBMW group had lower median CRP levels at baseline, their levels were above normal and consistent with their disease state. It is possible that age or gender differences between the groups may have affected CRP scores. Several IBD studies have found that the presence of rheumatoid disease increases CRP levels and reduces IBDQ.[48] Because the median age of the ES group was more than 9 years greater than the BBMW group, they may have had higher rates of rheumatoid disease. Larger studies would be needed to explore this possibility. IBD studies have also shown that women tend to score lower on IBDQ than men.[48] In the present study, the higher proportion of women in the ES group compared with the BBMW group was not associated with lower mean baseline IBDQ scores. Again, this may have been because of the small sample size. Considering the wide range of baseline CRP scores, ES (minimum 169.4, maximum 26,200.0) versus BBMW (minimum 123.8, maximum 17,480.0), it would be difficult to explain this discrepancy based on such a small sample size.

Records of home practice hours and attendance at follow-up sessions were incomplete and could not be analyzed. In a larger study, maintaining such records might demonstrate relationships between at-home practice, group follow-up attendance, and outcomes.

CONCLUSIONS

Participation in the BBMW was associated with significant subacute and long-term improvements in psychological symptoms (anxiety, depression, perceived disability, and

perceived stress), physical symptoms (bowel symptoms, systemic symptoms, and pain), and quality of life (daily function and social function) in patients with IBD. Concomitantly, participants in the BBMW had significant reductions in CRP, an inflammatory marker after 26 weeks. Mind–body practices can be taught as adjunctive treatments to groups of patients, thereby reducing cost and time demands on health care providers. Interventions, such as BBMW, that emphasize slow VRBPs may provide an effective, safe, low risk cost-effective method to improve symptoms, quality of life, and inflammation in IBD. Additional studies with larger groups and longer follow-ups are warranted to validate and extend these encouraging results.

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