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Original Article

Anxiety disorder in menopausal women and the intervention efficacy of mindfulness-based stress reduction

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Abstract: Objectives: The purpose of this study was to investigate the current situation of anxiety disorder in menopausal women and to analyze the intervention effect of Mindfulness-Based Stress Reduction (MBSR). Methods: A total of 489 patients diagnosed with menopausal syndrome from July 2021 to June 2022 were selected as the study object. There were 120 patients with menopausal syndrome complicated with anxiety who were screened out by the Generalized Anxiety Disorder (GAD-7). The patients were divided into an experimental group (62 cases) and a control group (58 cases) according to the random number table method. The experimental group received MBSR intervention, and the control group received routine intervention. The present situation of menopausal women's anxiety disorder was analyzed. The Five Facet Mindfulness Questionaire (FFMQ) score, GAD-7 score, follicle stimulating hormone (FSH), estradiol (E2), and 5-hydroxytryptamine (5-HT) levels of the two groups were compared. Results: After a statistical analysis, it was found that the incidence of anxiety in patients with menopausal syndrome was 24.54% (120/489). The severity of menopausal syndrome was positively correlated with the degree of anxiety ($r = 0.621$, $P<0.001$). After the intervention, in comparison with the control group, the FFMQ score was higher and the GAD-7 score was lower in the experimental group. The levels of FSH were decreased, and the levels of E2 and 5-HT were increased in both groups, with more significant alterations in the observation group (all $P<0.05$). Conclusions: The incidence of anxiety disorder in menopausal women was high and its severity was related to the severity of menopausal syndrome. MBSR intervention can alleviate anxiety symptoms and improve hormone levels in the patients.

Keywords: Menopausal, anxiety disorder, mindfulness-based stress reduction, effect

Introduction

Perimenopause refers to the transition from regular menstruation in the reproductive period to menopause. The duration is from the occurrence of clinical features and changes (endocrinology and biology) related to decreased ovarian function to one year after the last menstruation [1]. This stage can begin at the age of 40 and last as short as 1 to 2 years and as long as more than 10 years. This is an inevitable physiological stage for women and can be accompanied by a drop in physiological estrogen levels. Approximately 15% to 50% of perimenopausal and postmenopausal women may experience a range of psychological and emotional symptoms, such as anxiety, depression, insomnia, and forgetfulness. Most of the symptoms are physical symptoms. They can easily cause missed diagnosis and misdiagnosis, resulting in the unsatisfactory therapeutic effect of menopausal syndrome for some women [2]. In recent years, with the deepening of related research, these problems are paid more extensive attention. Relevant studies have shown that compared with natural menopause (caused by the depletion of follicles in the ovary or loss of response of the remaining follicles to gonadotropin, follicles no longer develop and secrete estrogen [3]), artificial menopause (caused by ovarian function injury caused by surgical resection of bilateral ovaries, radiation therapy, and

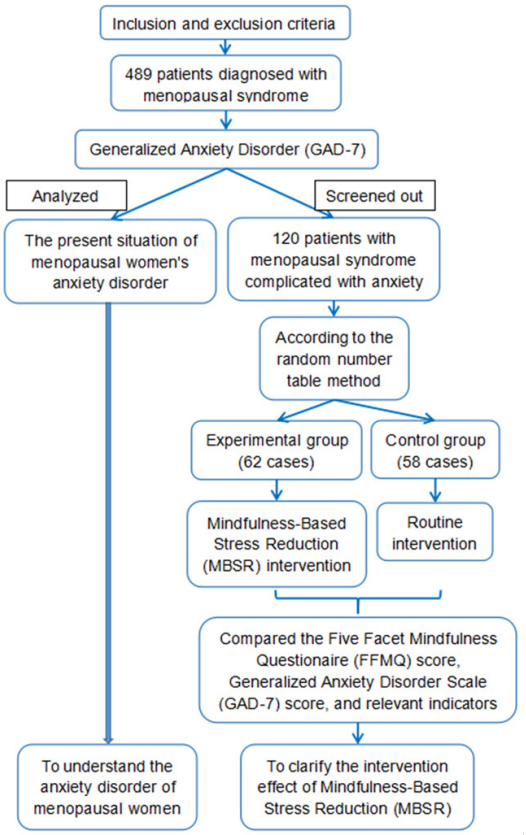

Figure 1. The flow chart of this research design. There were 489 patients diagnosed with menopausal syndrome who were selected. A total of 120 patients with menopausal syndrome complicated with anxiety were screened out by Generalized Anxiety Disorder (GAD-7). According to the menopausal syndrome and anxiety, patients voluntarily choose different intervention methods and were divided into an experimental group (62 cases, MBSR intervention) and a control group (58 cases, routine intervention). The present situation of menopausal women's anxiety disorder was analyzed. The Five Facet Mindfulness Questionaire (FFMQ) score, Generalized Anxiety Disorder Scale (GAD-7) score, and hormone index levels of the two groups were compared.

chemotherapy [4]) is more likely to cause menopausal syndrome [5]. The menopausal syndrome refers to a series of mental and physical manifestations of perimenopausal women due to decreased sex hormone content. We speculated that the occurrence of menopausal syndrome, changes in hormone levels, and psychological factors are important reasons. Studies show that [6] the prevalence of mood disorders worldwide is 9.5% in women and 5.8% in men. As a common mental disorder, the prevalence rate of anxiety is 1.9% to 5.1% in the middle age of the general population. In the 45-55 years old population–the proportion of female patients is twice that of male patients [7]. Perimenopause poses unique challenges to women's physical and mental health. When the traditional biomedical model is transformed into a bio-psycho-social medical model, and China enters the aging stage, we propose the following views: The Generalized Anxiety Disorder Scale (GAD-7) is used to actively screen the anxiety disorder of perimenopausal women in the outpatient department, to identify the mental and psychological factors associated with physical symptoms in the early stage. Mindfulness-Based Stress Reduction (MBSR) [8]-based group counseling is an intervention method to rapidly open patients' inner channels, help them to carry out cognitive reconstruction, reduce adverse emotions, and improve their social functions. MBSR can reduce the psycho-neurological symptoms of patients, ensure physical and mental health to the maximum extent, and improve the quality of life [9]. There are few studies on the application of this method in menopausal syndrome patients with anxiety disorder. Based on the above research background, the purpose of this study was to explore the status quo investigation of anxiety disorders in menopausal women and the effect of an intervention, to provide a practical basis for the inclusion of anxiety screening and intervention in routine menopause outpatient work.

Material and methods

Selection of suitable research subjects

The flow chart of this research design is shown in **Figure 1**. Menopausal syndrome patients diagnosed with an anxiety disorder from July 2021 to June 2022 were selected.

The following criteria must be met for inclusion (inclusion conditions): (1) The outpatient diagnosis of the menopausal syndrome; (2) GAD-7 was evaluated as an anxiety disorder; (3) Sign informed consent. Patients with the following conditions were excluded (exclusion option): (1) Abnormal menstruation caused by pathological diseases; (2) Serious substantial lesions of the heart, liver, and kidney; (3) Complicated with a malignant tumor. A total of 489 patients were included. This study was approved by the Medical Ethics Committee of Dalang Hospital of Dongguan.

Table 1. GAD-7 Psychological Scale

Question	Not at all	Several days	More than a week	Almost every day
Feeling nervous, anxious, or eager.	0	1	2	3
Inability to stop or control worry.	0	1	2	3
Worry too much about a variety of things.	0	1	2	3
Difficulty to relax.	0	1	2	3
Unable to sit sedentary due to restlessness.	0	1	2	3
Easily become annoyed or irritable.	0	1	2	3
Fear something terrible will happen.	0	1	2	3

Diagnostic criteria

Menopausal syndrome diagnostic criteria: Refer to the Chinese Obstetrics and Gynecology [10] menopausal syndrome-related standards, clinical manifestations of mild symptoms of hot flashes, sweating, lasting ≥2 min, severe cases appear multiple times within 1 day, night, stress state prone; skin thinning, itching, and walk feeling; depression, insomnia, excitement, anxiety; palpitation, false angina, chest tightness; joint deformation, back pain, night cramps; vaginal dry itching, difficulty in sexual intercourse, frequent urination and urgency; and follicle-stimulating hormone and luteinizing hormone increased, estradiol decreased.

Screening of patients with anxiety disorders

The Generalized Anxiety Disorder (GAD-7) was used to assess the anxiety of patients. Menopausal patients with anxiety were screened out.

GAD-7 Psychological Scale scoring criteria [11]: The self-rating anxiety scale based on the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) (**Table 1**), consisted of 7 items. Each of them are composed of 4 choices; Not at all, several days, more than a week, and almost every day. Scores ranged 0, 1, 2, and 3 out of 21. Results Analysis: The total score of 0-4 was no anxiety, 5-9 was mild anxiety, 10-14 was moderate anxiety, and 15 or above was severe anxiety. Gpad-7 scale score ≥5 was diagnosed as anxiety disorder.

Grouping and intervention methods

Patients with menopausal syndrome and anxiety disorder were divided into an experimental group (mindfulness-based stress reduction therapy intervention) and a control group (routine intervention) according to the random number table method. Both groups received basic treatment on the day of admission, including hemostasis, menstrual cycle adjustment, and endometrial disease prevention.

Control group: Routine intervention was performed based on basic treatment, including routine health education and psychological nursing, all of which were performed by the responsible nurse. The intervention was performed once a week for 8 weeks.

The experimental group was provided with MBSR intervention based on basic treatment. Specific methods: The patients were organized to perform group MBSR activity once a week. Each activity lasted for 1 hour, for 8 weeks. During the activity, the patient's age, course of disease, symptoms, family background, and knowledge of the disease were understood. The patient was guided to self-perceive the changes of the disease symptoms and psychological emotions without making value judgments. The inducement factors, common symptoms, and treatment plan of menopause syndrome were explained in detail to the patient, so that the patient correctly understood the disease and could actively face their physical and psychological adverse reactions. Guidance on medication, diet, physical exercise, and health was provided. A list of successful cases was shared to improve patients' confidence in the treatment. Patients were guided to relieve anxiety through meditation, breathing training, and developing hobbies. The family members were advised to provide adequate emotional support and mental encouragement to the patient, reduce the anxiety and mental and neurological symptoms of the patient during perimenopause, and help the patient proceed through the perimenopause

smoothly. The intervention was performed once a week for 8 weeks.

Observation target

(1) Baseline data: Age, body mass index (BMI), duration of anxiety symptoms, educational level, marital status, occupational status, the severity of the menopausal syndrome, and degree of anxiety. (2) Evaluation criteria for the severity of menopausal syndrome: Using the modified Kupperman scale [12], the clinical manifestations of the menopausal syndrome were summarized into the following 13 symptoms: Hot flash and sweating, sensory disturbance, insomnia, excitations, depression and suspicion, vertigo, fatigue, joint pain, headache, palpitation, skin and sensation, decreased sex life, urinary system infection. Symptom score = weighted factor × degree score, the total score was 0-53 points. There were 13 weighted factors (basic points), with hot flashes and sweat scoring four points and the rest one or two points. Symptoms were scored on four scales: 0 (no symptoms), 1 (occasional symptoms), 2 (persistent symptoms), and 3 (affecting life). The sum of all symptom scores was the total score. Severity was classified according to the total score: 6-15 was mild, 16-30 was moderate, and ≥31 was severe. (3) Five Facet Mindfulness Questionaire (FFMQ): It is divided into five themes, observe, description, awareness, nonjudgmental, and inaction. The higher the total score was, the higher the level of mindfulness would be. (4) GAD-7 score. (5) Relevant indicators: Including serum follicle-stimulating hormone (FSH), estradiol (E2), and 5-hydroxytryptamine (5-HT). Assay methods: Before and after the intervention, 5 mL of forearm venous blood was collected in the early morning (8:00-8:30) of patients on an empty stomach (3-5 days of menstruation, before and after treatment of menopause). After centrifugation at 3000 r/min, the serum was collected and stored in the refrigerator for testing. Serum FSH and E2 levels were detected by Elecsys2010 electrochemical luminescence automatic immunoassay analyzer. The 5-HT level was determined by the double antibody sandwich method. The operation was strictly according to the instructions of the ELISA kit (provided by Shanghai Jianglai Biotechnology Co., Ltd.).

Sample size calculation method

This study was a randomized controlled trial. The experimental group was the MBSR in tervention group. The control group was the conventional intervention group. The inefficiency of the intervention of the subjects was the outcome index of the observation. According to the literature, it was expected that the inefficiency of the MBSR group was 30%. The inefficiency of the control group was 40%, the bilateral $\alpha = 0.05$ was set, and the test efficiency was 90%. According to the sample size calculation formula: $n = (\frac{2P \times (1 - P) \times (Z\alpha + Z\beta)^2}{(P1 - P2)^2})$. In the equation, P = (P1+P2)/2. Calculation results: Experimental group and control group each need 84 cases of research objects.

Statistical approach

SPSS 17.0 software was used for the statistical analysis of data in this study. Measured data were described by mean ± standard deviation and analyzed using a t-test. For intragroup before-after comparison, the paired sample t-test was used. the between-group comparison, the independent sample t-test was used. Count data were expressed as number (%) and analyzed using the chi-square test. The correlation between anxiety and the severity of menopausal syndrome was calculated by the Spearman correlation coefficient. The test level was $\alpha = 0.05$.

Results

A survey of anxiety disorders in menopausal women

A total of 489 patients with menopausal syndrome were selected, and 120 patients with menopausal syndrome complicated with anxiety were evaluated by the GAD-7 scale. The incidence of anxiety in menopausal syndrome patients was 24.54%. The severity of menopausal syndrome was positively correlated with anxiety ($r = 0.621$, $P<0.001$, **Table 2**).

Comparison of baseline data between groups

A total of 120 patients with menopausal syndrome and anxiety were screened, including 62 patients in the experimental group and 58 patients in the control group. Baseline data of

Table 2. Comparison of anxiety degree of patients with different symptoms of menopausal syndrome

Severity of menopausal syndrome	Number of cases	No anxiety	Mild anxiety	Moderate anxiety	Severe anxiety
Mild	23	0 (0.00)	11 (47.83)	8 (34.78)	4 (17.39)
Moderate	71	0 (0.00)	2 (2.82)	54 (76.06)	15 (21.13)
Severe	26	0 (0.00)	0 (0.00)	2 (7.69)	24 (92.31)
χ^2				69.994	
P				<0.001	

Table 3. Baseline data between the two intervention groups

Baseline information	Control group (n = 58)	Experimental group (n = 62)	t/χ^2	*P*
Age (years)	58.73±6.21	59.04±6.17	0.274	0.784
BMI (kg/m^2)			1.922	0.589
<18.5	3 (5.17)	1 (1.61)		
18.5-24.0	37 (63.79)	40 (64.52)		
24.1-28.0	11 (18.97)	10 (16.13)		
>28.0	7 (12.07)	11 (17.74)		
Duration of anxiety symptoms (months)	5.17±1.28	5.32±1.33	0.629	0.531
Degree of education			1.020	0.600
Junior High School and below	7 (12.07)	4 (6.45)		
High school or technical secondary school	28 (48.28)	31 (50.00)		
College degree or above	23 (39.66)	25 (40.32)		
Marital status			0.110	0.740
Have a spouse	40 (68.97)	41 (66.13)		
Have no spouse	18 (31.03)	21 (33.87)		
Vocational status			0.411	0.521
Be on the job	38 (65.52)	44 (70.97)		
No job	20 (34.48)	18 (29.03)		
Severity of menopausal syndrome			4.017	0.134
Mild	9 (15.52)	7 (11.29)		
Moderate	30 (51.72)	43 (69.35)		
Severe	19 (32.76)	12 (19.35)		
Degree of anxiety			0.754	0.385
Moderate	31 (53.45)	38 (61.29)		
Severe	27 (46.55)	24 (38.71)		

Not: BMI = body mass index.

the two groups were compared, and the results showed no statistical differences (*P*>0.05; **Table 3**).

Comparison of FFMQ score and GAD-7 score between two groups

After the intervention, in comparison with the control group, the FFMQ score was significantly higher and the GAD-7 score was significantly lower in the experimental group (all *P*<0.05; **Table 4**).

The scores of observation, awareness, and non-judgmental were all higher in the experimental group than those in the control group after the intervention (all *P*<0.05; **Table 5**; **Figure 2**).

Comparison of relevant indicators between the groups

After the intervention, the levels of FSH were decreased, and the levels of E2 and 5-HT were increased in both groups. Those changes were

Table 4. Changes of FFMQ scores and GAD-7 scores

Group	FFMQ scores		GAD-7 scores	
	before intervention	after intervention	before intervention	after intervention
Control group (n = 58)	112.38±3.07	111.45±3.15	14.28±2.16	11.26±2.56[a]
Experimental group (n = 62)	112.44±3.11	114.24±3.30[a]	14.39±2.01	8.13±1.82[a]
t	0.106	4.731	0.289	7.758
P	0.916	<0.001	0.773	<0.001

Note: [a]indicates that compared with the group before intervention, *P*<0.05. FFMQ = five factor measurement table, GAD-7 = Generalized Anxiety Disorder.

Table 5. Scores of FFMQ scales in each dimension of the groups

Group	Control group (n = 58)		Experimental group (n = 62)	
	before intervention	after intervention	before intervention	after intervention
Observation	24.82±1.46	24.78±1.38	24.67±1.24	25.57±1.32[B]
Description	25.76±1.88	24.80±1.96	25.65±1.64	24.77±1.77
Awareness	21.31±1.46	21.34±1.18	21.62±1.51	21.83±1.35[B]
Non judgmental	20.26±1.49	20.13±1.56	20.25±1.17	21.42±1.43[b,B]
Inaction	20.24±1.52	20.42±1.38	20.27±1.28	20.67±1.26

Note: [b]represents comparison with the same group before intervention, [B]represents comparison with the control group before the intervention, *P*<0.05.

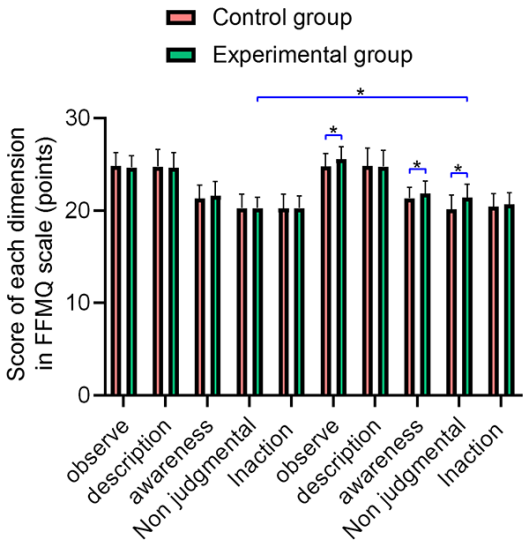

Figure 2. Scores of each dimension of FFMQ scale in the two groups. Note: *indicates the comparison of data between the two groups, P<0.05. FFMQ = five factor measurement table.

more significant in the experimental group (*P*<0.05; **Table 6**).

Discussion

Menopause is a necessary physiological process for women. After entering menopause, women's good mental state is more conducive to their health, social, and family harmony. Affected by the changes in endocrine status in the body, such as the decrease of physiological estrogen level, 15% to 50% of menopausal women have symptoms such as emotional instability, anxiety, and depression [13]. According to the statistics of this study, the incidence of anxiety in patients with the menopausal syndrome was 24.54%. This was like the results of related studies [14]. The incidence of anxiety in perimenopausal women was much lower than that reported in the literature (81.58%) [15] and higher than that reported in the literature (5.23%) [16]. This can be related to differences in research methods, regions, sample size, and inclusion criteria. This suggested that the incidence of anxiety in menopausal women in this study was at a high level.

This study found that the severity of menopausal syndrome was positively correlated with the severity of anxiety. This was consistent with relevant research results [17]. The more severe the symptoms of the perimenopausal syndrome, the higher the incidence of adverse mood [18, 19]. Menopause is the transition stage from the fertile period to old age. At this stage, women's ovarian function gradually declines, leading to menopause syndrome, often accompanied by a series of psychological changes. Due to the increase in age, changes

Table 6. Changes in the level of the two groups of relevant indicators

Group	FSH (mIU/mL)		E2 (ρg/mL)		5-HT (μmol/L)	
	before intervention	after intervention	before intervention	after intervention	before intervention	after intervention
Control group (n = 58)	45.63±3.36	41.55±4.58[c]	23.58±3.21	26.72±3.39[c]	0.63±0.20	0.75±0.22[c]
Experimental group (n = 62)	45.58±3.47	31.58±4.43[c]	23.72±3.15	34.57±4.16[c]	0.64±0.21	1.68±0.29[c]
t	0.080	12.120	0.241	11.290	0.267	19.690
P	0.936	<0.001	0.810	<0.001	0.790	<0.001

Note: [c]means compared with the group before the intervention, $P<0.05$. FSH = follicle stimulating hormone, E2 = estradiol, 5-HT = 5-hydroxytryptamine.

in a family and social environment increased physical burden. Menopausal women are prone to insomnia, over worry, anxiety, and adverse psychological problems. This aggravates the negative emotions of patients with menopausal syndrome.

The results of this study showed that MBSR intervention could significantly improve the level of mindfulness, relieve anxiety symptoms, and improve the hormone levels of patients. This was consistent with relevant research results [20]. A study [21] found that patients in the MBSR intervention group showed improvement in hot flashes, sweating, sensory disturbance, insomnia, excitability, fatigue, and palpitation. The total score of the modified Kupperman scale was significantly lower than before the intervention in the control group. This study suggested that MBSR could ameliorate the symptoms associated with menopausal syndrome in perimenopausal women. The effect of MBSR on the level of mindfulness and mood state has been proven [22]. In this study, the FFMQ scale was used to evaluate the mood state of the patients. The results showed that MBSR intervention significantly improved the observation, awareness, and non-judgmental level of the patients. There was no significant change in patients' description and inactivity, but the total FFMQ score was significantly improved. These results suggested that MBSR could improve some dimensions of FFMQ and improve the mindfulness level of patients. Through MBSR intervention, the degree of mindfulness of menopausal patients was improved correspondingly. Their perception of inner thoughts and emotions was clearer and was more conducive to their own out-of-the-negative thinking mode. It reduced the interference of anxiety, adverse events, and negative information. Studies [23] had shown that self-help MBSR could help improve menopausal symptoms, improve mindfulness, and improve negative emotions. Previous studies suggested that MBSR could improve depression and anxiety in menopausal women. MBSR was based on the theory of mindfulness stress reduction. Through meditation and body awareness, MBSR awakened individuals' inner focus and helped patients regulate their emotions, relieving pressure and pain and achieving the purpose of relieving anxiety symptoms [24]. In terms of neuro electrophysiology and imaging, foreign scholars had explained that MBSR could lead to the enhancement of signals in brain regions involved in emotional regulation [25]. In this study, after MBSR intervention, the FSH level of patients was higher than that before the intervention. The E2 and 5-HT levels were higher than that before the intervention. This was related to the improvement of the anxiety state of patients by MBSR. Positive emotions can regulate the endocrine changes of the body and improve physical and mental state and immune function [26]. Some studies had found that the endocrine changes of menopausal women were closely related to mood. They pointed out that a positive mood can make patients have good endocrine regulation, promoting the enhancement of body immunity and the improvement of physical and mental state [27]. Currently, there is no consensus on the mechanism of action of MBSR. Some scholars have found that MBSR training can increase the density of the anterior insula, hippocampus, and temporal lobe through magnetic resonance imaging (MRI) technology [28]. Long-term MBSR training can promote the decrease of amygdala activation [29] and transform the electrical activity of specific regions of the prefrontal cortex related to the emotional expression [30]. This study speculated that the effect of MBSR on menopausal

patients with anxiety can be the same as the above mechanism, but strong evidence was needed to confirm.

In conclusion, the incidence of anxiety disorder in menopausal women was high and its severity was related to the severity of the menopausal syndrome. MBSR intervention can alleviate anxiety symptoms and improve hormone levels in patients. This study was a single-center study, with deficiencies such as selectivity bias and small sample size. This would have an affect on the experimental results. It was necessary to expand the sample size and confirm the prospective randomized controlled experiment, to enhance the reliability of the conclusions of this study. Follow-up data of the subjects were not observed in this study. The long-term effects of MBSR intervention need to be studied.

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Disclosure of conflict of interest

None.

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