

The Effectiveness of Mindfulness-Integrated Cognitive-Behavioral Therapy on Sleep Quality, Anxiety, and Fatigue in Patients with Multiple Sclerosis: A Randomized Clinical Trial

Sahar Pouyanfard, Mohsen Mohammadpour, Aliakbar Parvizifard*, Aliakbar Foroughi

Department of Clinical Psychology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran

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Abstract

Background and Objective: Multiple sclerosis (MS) is a chronic disease, which results in numerous medical problems, as well as psychological symptoms such as anxiety, low sleep quality, and fatigue. These problems usually result in deterioration of clinical symptoms and low efficacy of the patients. The current study investigated the effectiveness of mindfulness-integrated cognitive-behavioral therapy (MICBT) on sleep quality, anxiety, and fatigue in patients with MS.

Materials and Methods: Twenty patients with MS were randomly assigned to MICBT or control groups. Data collection tools were Beck Anxiety Inventory (BAI), Pittsburgh Sleep Quality Index (PSQI), and Fatigue Severity Scale (FSS). Measurements were performed in three stages including before the intervention, after the end of the intervention, and in a follow-up phase. One-way analysis of covariance (ANCOVA) was performed with SPSS to compare the results between the two groups.

Results: A significant reduction in anxiety ($d = 0.62$) and fatigue ($d = 0.56$) and a significant increase in sleep quality ($d = 0.56$) were observed in the experimental group compared to the control group ($P < 0.05$). The results also were kept in follow-up phase.

Conclusion: MICBT is effective on the anxiety, sleep quality, and fatigue in patients with MS. As a result, mental health professionals can take advantage of this treatment to address the psychological problems of these patients.

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Keywords: Multiple sclerosis; Mindfulness; Cognitive behavioral therapy; Sleep

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Introduction

Multiple sclerosis (MS) is an inflammatory chronic autoimmune disease of the central nervous system (CNS) (1, 2). It is estimated that about 2-3 million people are affected by MS worldwide, with the highest prevalence among women (3). MS affects many life domains such as work, family functioning, education, and social interaction (4). The prevalence of psychiatric and psychological symptoms in patients with MS has been reported in several studies (5, 6). Comorbid psychological disorders with MS are associated with

weaker life quality, notable pain, and higher utilization of health care services (7, 8).

The prevalence of anxiety among patients with MS ranges from 19% to 90% (9), and some studies have shown that anxiety occurs more frequently than depression (10). Anxiety and stress are correlated with more severe forms of the disease, and consequently, represent more severe forms of demyelination (11, 12).

Fatigue is the most common and debilitating symptom in patients with MS that has been reported to affect 50-80 percent of patients (13, 14). Fatigue affects mood, sleep, and life quality of these patients (15). In addition, comorbid anxiety in these patients is associated with more fatigue (8, 16).

* **Corresponding author:** A. Parvizifard, Department of Clinical Psychology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran
Tel: +98 918 330 8692, Fax: +98 21 3427647
Email: parvizia@yahoo.com

Patients with MS have significantly more sleep problems than the general population (17). Research has shown that about 50 percent of patients with MS report sleep problems (18). These sleep problems can be the result of clinical manifestation of the diseases such as pain, muscle spasms, and anxiety (18, 19), and at the same time, it can cause these symptoms (20). Fatigue can be related to sleep disorders in patients with MS, and the patients have usually twice as many problems with sleep quality as in the control group (21-23).

Different psychological treatments have emerged to manage comorbid psychological problems in patients with MS (4, 24). One of these treatments is Cognitive Behavioral Therapy (CBT), which its moderate effects on treatment of comorbid depression and anxiety have been previously confirmed (4, 25). Lack of improvement in emotion regulation skills, inability to increase and tolerate pain acceptance, and lack of rapid responses are the main limitations of CBT. For this reason, Mindfulness-Based Interventions (MBI) have emerged to resolve these limitations (26). One of these interventions is mindfulness-integrated CBT (MICBT), which integrates mindfulness-based techniques with CBT (27).

The purpose of this integration is to educate the patients to have the ability to adjust their emotion and attention and use these skills for managing their problems. One of the major objectives of MICBT is to treat comorbid psychological problems such as anxiety and depression (28). MICBT effectiveness has been proven in various studies (29-31). Bahrani et al. examined the effectiveness of MICBT on depression, anxiety, and stress in female patients with MS (32). The experimental group received eight 2-hour sessions of MICBT, while the patients in the control group continued treatments under the supervision of a neurologist. The results of the study showed the efficacy of MICBT treatment. They advised that future studies assess the effect of MICBT on both male and female patients with MS over follow-up periods (32). Considering the efficacy of MICBT on the comorbid psychological symptoms such as anxiety in patients with MS and the limitation of previous studies, and regarding that, based on our knowledge, the effectiveness of MICBT has not yet been studied on the quality of sleep and fatigue of these patients, the aim of the current study was to examine the effectiveness of MICBT treatment on sleep quality, anxiety, and fatigue

among patients with MS

Materials and Methods

Participants

The study participants were selected from all patients with MS who referred to Shafa Hospital, Kermanshah, Iran, from February 2018 to April 2018. Patients were referred to the clinical psychology department by a neurologist to participate in the study. Finally, 20 people were selected based on inclusion and exclusion criteria and were randomly divided into two groups. The inclusion criteria were patients suffering from confirmed MS (recurrent or subtractive) by a neurologist, diagnosis confirmation using diagnostic methods [e.g., magnetic resonance imaging (MRI)], being under treatment, aged between 18-50 years, having at least a high school educational level, and willingness to participate in the study. The exclusion criteria included comorbid physical illnesses, psychosis and delirium occurring during the treatment course, severe arousals (e.g., extreme anger, uncontrolled restlessness, or impulses), change in the dose and type of medications used during the study due to oscillation of the symptoms of the patient, and receiving other psychological treatments during the course of research. Patient allocation is depicted in figure 1.

Measures

Pittsburgh Sleep Quality Index (PSQI)

PSQI is a validated questionnaire, which evaluates the sleep quality over the last month. It includes 19 individual items with seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction with score from 0-3 for each section and with total score of 21. Higher scores (6 and above) indicate poor sleep quality (33). The validity of PSQI was evaluated with Cronbach's alpha of 0.80 and its test-retest reliability ranged from 0.93 to 0.98 (34).

Beck Anxiety Inventory (BAI)

BAI is a self-report questionnaire that measures anxiety. The questionnaire is based on 21 anxiety symptoms and is graded from 0 to 3 according to the Likert scale. A higher score indicates more severe anxiety. This questionnaire emphasizes the physiological aspect of anxiety. The three subscales are concerned with anxiety, the other three are related to specific phobias, while other question measures the auto-hyperactivity and motor stress of anxiety.

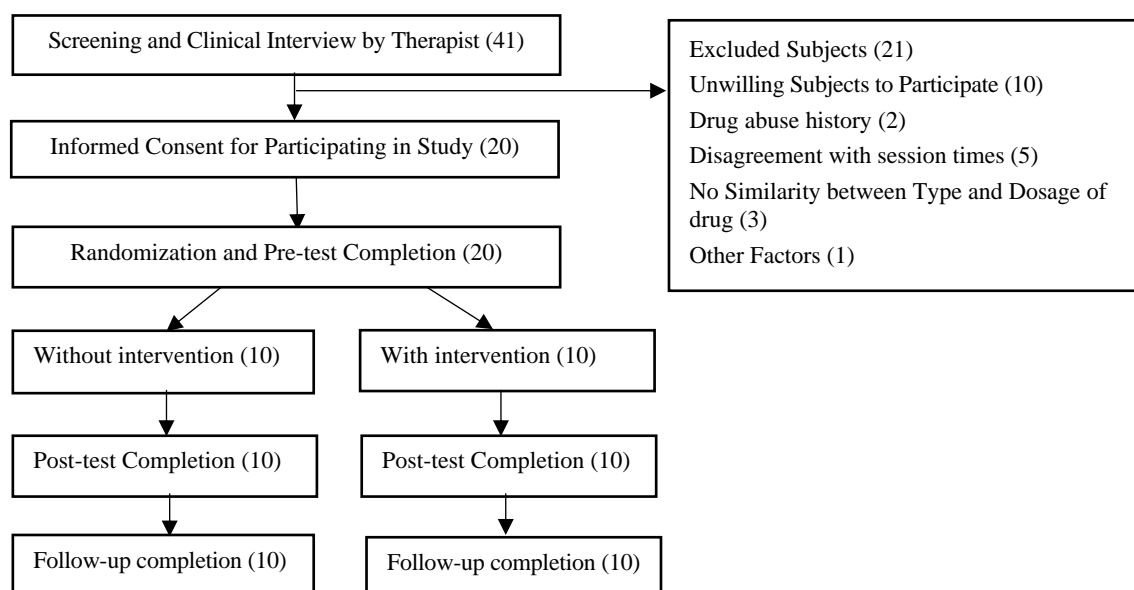


Figure 1. The research flowchart

The original version of the questionnaire has good psychometric properties (35). Hossein Kaviyani and Mousavi examined the psychometric adequacy of this questionnaire in Iran (36).

Fatigue Severity Scale (FSS)

This scale is designed and reviewed by Krupp et al. (37) to measure fatigue severity in patients with MS and lupus. The scale consists of 9 items, which is extracted from 28 items of fatigue questionnaire. The researchers assessed the reliability and validity of this scale in patients with MS and lupus. Cronbach's alpha was 0.88 in healthy subjects, 0.81 in patients with MS, and 0.89 in patients with lupus. They also reported that this scale had a high degree of internal consistency (37). The validity of the Persian version of this test was measured by the test-retest method and the results indicated a Cronbach's alpha of 0.98 and a test-retest reliability of 0.93 (38).

Design

This study was a semi-experimental clinical trial with control and experimental groups approved by the Iranian Registry of Clinical Trials (IRCT) committee (approval code: IRCT201601030258N4). The authorities of Shafa Hospital in Kermanshah were initially requested to explain the purpose of research to study participants and introduce them to the researchers. Then, the initial assessments on the patients were performed to evaluate their accordance with the inclusion and exclusion criteria of the study by an independent evaluator. The individuals who met the inclusion criteria of the study provided an

informed consent form and joined the project. A sample size of 20 patients with MS were randomly divided into experimental and control groups. The control group received usual treatment, while the intervention group participated in MICBT sessions as well as drug therapy. Treatment program was provided to the experimental group for 8 sessions of two hours. Post-test measurements were conducted after providing the intervention and the follow-up stage was conducted two months after the completion of the treatment. The intended intervention in this study was extracted from the current book of practicing MICBT (the principles and method of implementation), developed by Cayoun (27). The intervention was performed by an MSc student in clinical psychology (first author) who had received specialized training in this area under the supervision of a PhD graduate in clinical psychology.

Statistical analysis

Data were analyzed by SPSS software (version 24, IBM Corporation, Armonk, NY, USA). Descriptive analyses [mean and standard deviation (SD)] and one-way analysis of covariance (ANCOVA) were used. Before analyzing the covariance of the related assumptions, the regression slope, the default error variance equation, the linear assumption of regression, and the relationship between the regression and the normality assumption were investigated.

Ethical considerations

All participants were aware of the study conditions.

Table 1. The curriculum for mindfulness-integrated cognitive-behavioral therapy (MICBT) sessions

1	An overview of MICBT, the flow of the program, and the contents of the next sessions
2	The basic principles of mindfulness, the components of CBT, and mindful breathing
3	Part-by-part body scanning (continued), explaining about body sensations, informal practice
4	Body scanning exercises (continued), behavior therapy techniques (such as problem solving), and the relationship of mindfulness with CBT
5	Body scanning exercises (continued), review of SUDS
6	Interpersonal skills, assertiveness, and role play
7	Introducing the concepts of compassion and empathy, loving-kindness meditation
8	Review and evaluation

CBT: Cognitive-behavioral therapy; SUDS: Subjective Units of Distress Scale

Ethical considerations and explanations of research were presented to the patients at the meeting. The informed consent form was filled out by all the participants and they were assured that their results and identity would remain confidential, and under no circumstances would their health information be provided to any person except the medical staff. This study was approved by the Ethics Committee of Kermanshah University of Medical Sciences (KUMS.REC.1396.616).

Intervention

The MICBT includes internalization and extermination skills and consists of four steps as follows: 1) the individual stage, 2) the stage of exposure, 3) the interpersonal stage, and 4) the stage of creating love and kindness for one's self and others; it includes eight treatment sessions. Two introductory sessions were held prior to the main sessions to familiarize group members with the process of group therapy. At the first meeting, MICBT was introduced to the subjects, explaining that it aims to create a commitment to daily practices. The mindfulness principles were explained to the patients and a clear explanation of treatment was presented to them. In the second session, the most important mechanisms were introduced. The third session provided a visceral insight and intellectual equilibrium to the study participants. In the fourth session, the second phase was introduced. In the fifth session, the second stage continued at

the most challenging level and the third stage was introduced. The sixth session consisted of the introduction of assertiveness skills and role-playing as a means of encounter. In the seventh session, the fourth stage was introduced, and at the eighth session, the fourth phase was consolidated and the entire intervention program was reviewed (27, 28). The contents of the treatment sessions are provided in table 1.

Results

Descriptive findings of research: Table 2 represents demographic characteristics of the study subjects. Accordingly, there were 8 men (4 in the experimental group and 4 in the control group), and 12 women (6 in the experimental group and 6 in the control group). The educational level was as follows: Experimental group: under high school (n = 1), high school (n = 2), associate degree (n = 1), bachelor degree (n = 4), and master degree (n = 2). Control group: under high school (n = 1), high school (n = 2), associate degree (n = 0), bachelor degree (n = 5), and master degree (n = 2).

Results of mean and SD for research variables in the experimental and control groups at pre-test, post-test, and follow-up phases are shown in table 3. Accordingly, the intensity of anxiety and fatigue significantly decreased in the intervention group more than the control group. In addition, sleep quality increased in the intervention group.

Table 2. Demographic characteristics of study participants

Variable	Category	Experimental group (n = 10)	Control group (n = 10)
Gender*	Male	4 (40)	4 (40)
	Female	6 (60)	6 (60)
Education level*	Under high school	1 (10)	1 (10)
	High school	2 (20)	2 (20)
	Associate degree	1 (10)	0 (0)
	Bachelor degree	4 (40)	5 (50)
	Master degree	2 (20)	2 (20)
Age (year)**	Male	31.75 ± 4.27	35.50 ± 5.68
	Female	37.17 ± 4.95	30.17 ± 4.53

*Data is presented as number (percent); **Data is presented as mean ± standard deviation (SD)

Table 3. Mean and Standard deviation (SD) for sleep quality, anxiety, and fatigue

	Experimental group			Control group		
	Pretest (Mean ± SD)	Posttest (Mean ± SD)	Follow-up (Mean ± SD)	Pretest (Mean ± SD)	Posttest (Mean ± SD)	Follow-up (Mean ± SD)
PSQI	19.37 ± 2.12	12.37 ± 2.13	11.22 ± 3.70	18.22 ± 1.11	19.25 ± 1.58	19.68 ± 1.19
BAI	51.37 ± 4.59	26.75 ± 5.03	28.12 ± 4.25	50.37 ± 4.06	49.75 ± 4.62	48.75 ± 5.00
FSS	39.12 ± 4.36	21.25 ± 6.11	23.75 ± 5.62	36.50 ± 5.10	37.60 ± 5.68	34.12 ± 3.24

PSQI: Pittsburgh Sleep Quality Index; BAI: Beck Anxiety Inventory; FSS: Fatigue Severity Scale; SD: Standard deviation

The research hypotheses: To determine whether the obtained data estimate the underlying assumptions of ANCOVA, they were examined prior to analysis of hypothesis data; the results approved conducting ANCOVA. The results of Levene's test showed the equality of variances for sleep quality ($f = 0.13$, $P = 0.21$), anxiety ($f = 0.15$, $P = 0.10$), and fatigue ($f = 0.20$, $P = 0.70$). According to the Kolmogorov-Smirnov test (K-S test), the distribution of data was normal for sleep quality ($Z = 0.725$, $P = 0.669$), anxiety ($Z = 0.551$, $P = 0.922$), and fatigue ($Z = 0.802$, $P = 0.541$). To investigate the obtained results, one-way ANCOVA was used. The post-test results of one-way ANCOVA are presented in table 4 and the same for the follow-up phase are listed in table 5.

Table 4. Analysis of covariance (ANCOVA) results: sleep quality, anxiety, and fatigue scores in post-intervention phase (between groups)

	SS	df	MS	F	P-value	ES
PSQI	117.82	1	117.82	31.63	0.001	0.56
BAI	2162.41	1	2162.41	100.7	0.001	0.62
FSS	717.44	1	717.44	36.27	0.001	0.56

PSQI: Pittsburgh Sleep Quality Index; BAI: Beck Anxiety Inventory; FSS: Fatigue Severity Scale; df: Degree of freedom; SS: Sum of squares; MS: Mean square; ES: Eta squared

Following the results of table 3 and assessing mean values for experimental and control groups in post-experimental groups from table 2, it can be concluded that post-intervention MICBT was successful in reducing depression and anxiety score and improving life expectancy score. The results in table 4 showed that the difference between the two groups in sleep quality ($P < 0.001$, $F = 31.63$, $d = 0.56$), anxiety ($P < 0.001$, $F = 100.75$, $d = 0.62$), and fatigue ($P < 0.001$, $F = 36.27$, $d = 0.56$) were significant in the post-test phase. This can be interpreted as effectiveness of MICBT in reducing mean score for depression and anxiety in post-intervention phase and improving life expectancy in this phase.

The results in table 5 showed that the

difference between the two groups in the sleep quality ($P < 0.002$, $F = 14.12$, $d = 0.52$), anxiety ($P < 0.001$, $F = 89.19$, $d = 60$), and fatigue ($P < 0.001$, $F = 34.22$, $d = 59$) were also significant in the follow-up phase.

Table 5. Analysis of covariance (ANCOVA) results for sleep quality, anxiety, and fatigue scores in follow-up phase

	SS	df	MS	F	P-value	ES
PSQI	102.02	1	102.02	14.12	0.002	0.52
BAI	1746.10	1	1746.10	89.19	0.001	0.60
FSS	1021.99	1	1021.99	34.22	0.001	0.59

PSQI: Pittsburgh Sleep Quality Index; BAI: Beck Anxiety Inventory; FSS: Fatigue Severity Scale; df: Degree of freedom; SS: Sum of squares; MS: Mean square; ES: Eta squared

Discussion

The purpose of the present study was to evaluate the effectiveness of MICBT on sleep quality, anxiety, and fatigue in patients with MS. The results of this study showed that MICBT produced moderate effects in patients with MS. This was in line with the results of the previous studies (24, 32, 39-42). In a study conducted by Grossman et al., MBI training was used for patients with MS. The results showed that MBI training reduced the severity of depression, anxiety, and fatigue and improved quality of life. Therapeutic effects were maintained for follow-up of 6 months (43).

The results of the present study showed that MICBT significantly increased sleep quality in the experimental group. This finding is consistent with other studies (40, 44, 45). In explaining this finding, it can be said that in the mindfulness training of watching breathing technique and homework, the mindfulness of breathing during the day and before sleep improves the quality of sleep. Mindfulness also teaches individuals how to quit their habits and to shift information processing by focusing on breathing. Hence, mindfulness teaches people to interact differently with their thoughts and feelings about sleep control (27, 28). Also, mindfulness involves principles such as being in the moment, preventing mental ruminations, controlling daily events, recognizing patterns of thoughts with a focus on breathing, pay-

ing attention to faulty cognition, and using acceptance and confrontation with thoughts. In poor sleep quality and insomnia, these components are impaired (27, 46). Therefore, it seems that mindfulness improves sleep quality by targeting the roots of insomnia and low sleep quality. Also, cognitive-behavioral techniques have helped to improve the quality of sleep by eliminating the roots of insomnia such as inability to accept and confront thoughts and lack of control over daily events.

The present study also revealed that the MICBT significantly reduced anxiety in the experimental group, compared with the control group; which this effect continued until the follow-up phase. These findings are consistent with other studies (24, 32, 39, 40, 42). Therefore, it seems that mindfulness skills training can help reduce anxiety in several ways. First, it teaches skills to see mental states such as worries, anxiety, and rumination as transient rather than real situations (47). Second, mindful breathing teaches individuals how to stay away from the inner troublesome experiences and distressed thoughts at the moment (48). Third, body scanning leads to awareness and acceptance of bodily sensations in everyday situations (27).

In addition, assertive training and role-playing as confronting measures could improve the preparation to coping with disease-related changes and life, and decrease the feeling of incapability; also it could improve the self-confidence of experimental group members to cope with the undesired conditions (49).

Fatigue was also significantly reduced in the experimental group of the current study. These results are consistent with other studies (40, 43, 50). In explaining this finding, it can be concluded that MICBT with increasing awareness of patients about negative thoughts and cognitive errors and its effect on fatigue intensity and also training coping strategies with these thoughts can affect the severity of fatigue in patients. It can also be explained by principles such as being present, observing without judgment, acceptance, raising awareness of experience, and creating adaptive responses. The continuation of mindfulness exercises leads to the acceptance of the illness by the affected person and changes in behavior for self-care and thus reduces the feeling of fatigue. Because individuals usually tend to avoid intrusive subjective experiences, by using mindfulness exercises, people respond differently to anxiety.

Therefore, mindfulness exercises increase distress tolerance, prevent habitual avoidance and ultimately adaptive self-regulation, and improve the healthy functioning of the mind-body, which is a barrier to fatigue (27, 43, 46).

The current study contained some limitations. The sample size was small, although consistent with other studies. The 2-month follow-up period may not be sufficient to assess the long-term maintenance of treatment gains. Further studies are recommended with long follow-ups. Boredom and fatigue of patients with MS may have affected the results of the current study. Future studies require controlled trials with larger samples and more facilities to eliminate boredom and fatigue of patients in one study.

Conclusion

This study provided further evidence for the effectiveness of the MICBT. Patients with MS face a variety of stressors in everyday life, as well as the stress related to their disease. Due to the effect of MICBT on reducing anxiety and fatigue and increasing the quality of sleep, and also with regard to psychological symptoms in these patients, the results of this study may be beneficial in treatment programs and services for patients with MS to improve sleep quality and reduce anxiety and fatigue.

Conflict of Interests

Authors have no conflict of interests.

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