Original Article

The effectiveness of mindfulness-based cognitive therapy in depression and serum cortisol levels in women with breast cancer and depressed women

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Abstract

Introduction: This study aims to investigate the effectiveness of mindfulness-based cognitive therapy in depression and serum cortisol levels in women with breast cancer and depressed women.

Materials and Methods: In this clinical trial, 30 women with breast cancer who referred to Omid Hospital, Mashhad-Iran and 30 women with depression who referred to counseling clinics of Mashhad in 2020-2021 were selected by the convenience sampling method and were randomly assigned to four equal groups (2 experimental groups and 2 control groups). The experimental groups received mindfulness-based cognitive therapy during eight 90-120 minute sessions per week, while the control group did not receive any intervention. Research instruments included the Depression Inventory (BDI-II) and the blood samples to evaluate the cortisol levels. Data were analyzed through descriptive statistics, and the covariance analysis.

Results: The results of depressed people demonstrated that mindfulness-based cognitive therapy is effective to reduce depression and serum cortisol levels within the normal laboratory range ($P < 0.001$). Further, the findings of breast cancer women indicated that mindfulness-based cognitive therapy reduced depression and increased serum cortisol from low to moderate levels within the normal laboratory range ($P < 0.001$).

Conclusion: Mindfulness-based cognitive therapy can be effective in neurobiological mechanisms in addition to improving psychological symptoms in depressed individuals and cancer patients.

Keywords: Cancer, Cortisol, Depression, Mindfulness-based cognitive therapy

Introduction

About 2.1 million women are diagnosed with breast cancer each year. This type of cancer is the second leading cause of cancer death in women after lung cancer. In 2018, it has been estimated that 627,000 women die from cancer, which is about 15% of all cancer deaths among women. According to estimates, the prevalence of breast cancer will increase from two million patients in 2018 to more than three million patients in 2046, which indicates a 46% increase (1).

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Depression, anxiety, fatigue, and fear of recurrence are commonly seen in cancer patients, but are often neglected and non-teated. In these patients, a positive feedback loop between stress and mood changes can be considered (2).

Meta-analytic studies in 12 countries in 2019 indicated that prostate cancer (27.17%), ovarian cancer (25.34%) and lung cancer (13.1%) had the lowest prevalence of depression, respectively, and breast cancer (42.5%) had the highest prevalence of depression in the studied countries (3).

On the other hand, Major Depressive Disorder (MDD) is a complex and multi factorial clinical syndrome characterized by physical, psychological and behavioral symptoms, which mainly include depressed mood, loss of energy and interest, suicidal thoughts, reduced quality of life and occupational-educational-family dysfunction, and by 2030, it will have the largest share in the global burden (4).

Exposure to chronic stress can lead to a maladaptive response that is mainly characterized by disruption of neuroendocrine regulation (increased cortisol) and the sympathetic nervous system (5). For example, chronic stress may lead to higher- or lower-than-normal cortisol levels in people with breast cancer, and both types can have important negative effects on health (6).

Studies have shown that in people with untreated MDD, there is a significant increase in the cortisol plasma level compared to healthy people (7). Mindfulness-based approaches have recently provided strong evidence in the care of depression and chronic illness. Mindfulness-based interventions promote specific attitudes such as acceptance, non-judgment, abandonment, patience and openness to current experience. The most common of these methods are Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT) (8). On the other hand, it should be noted that mindfulness meditation and mind-body exercises, by relying on the acquisition of positive coping styles, can induce and inform the related changes in the brain regions involved in the response to stress and in the symptomatology of depression by increasing the immunity level of patients (9).

Evidence from the neurobiology also suggests that mindfulness-based training can alter brain function and structure due to neuroplasticity. Some of the main neurological mechanisms include the effectiveness of mindfulness-based interventions such as attention control, emotion regulation and self-awareness. These interventions may also improve aspects of emotion processing such as emotion intensity, emotional memory, and emotional attention bias (10).

The main purpose of this study is to evaluate the effectiveness of mindfulness-based cognitive therapy in depression and serum cortisol levels among women with breast cancer and depressed people.

Materials and Methods

In this clinical trial, 30 women with breast cancer who referred to Omid Hospital, Mashhad-Iran and 30 women with depression who referred to counseling clinics of Mashhad in 2020-2021 were selected by the convenience sampling method and were randomly assigned to four equal groups (2 experimental groups and 2 control groups).

The subjects in the two groups of breast cancer patients and depressed people were selected in such a way that the officials of the Cancer Prevention Research Center in Omid Hospital and their colleagues in private counseling clinics referred the patients to the researcher and they participated in the study based on their consent and inclusion and exclusion criteria. Accordingly, 60 people were selected and randomly assigned to four groups (2 experimental groups and 2 control groups).The sample size is approximately 15 people for each group based on Cohen's formula and the opinions of statistical experts (11).

The subjects were divided into two experimental and control groups based on simple randomization through a table of random numbers in two separate groups of breast cancer patients and depressed people. To use the table of random numbers, the statistical population framework amounting to 30 people was initially determined in both groups and they were given a two-digit code, respectively. Then, the same number of digits was selected in the row or column direction. This continued until 30 cases in each group were selected as the sample. The subjects were tested individually before and after the treatment period using the Beck Depression Inventory (BDI-II) under the same conditions. Blood samples were taken between 8 and 10 am before the start of the first treatment session and after the last treatment session.

The inclusion criteria included women with clinical diagnosis of stage 0-3 for breast cancer based on clinical findings of cytology and physician diagnosis, consent to participate in the study, aged between 18 and 75 years, major depressive disorder based on DSM-V, a score between 20 and 28 in the Beck Depression Inventory-II, middle school education and higher. The exclusion criteria included metastasis to other parts of the body including liver, kidney and brain, schizophrenia spectrum and other psychotic disorders, bipolar and related disorders, substance use disorders, the use of psychotropic drugs and antidepressants, a history of participation in a mindfulness program during the implementation of the project, common meditation or yoga exercises during the last three months before joining the study. Then, the MBCT group received eight sessions of 90 to 120 minutes per week by a trained and experienced clinical therapist, and the patients in the control group did not receive any intervention during the eight sessions. Patients' depression was moderate, and delay in treatment was allowed for patients who did not receive any intervention during eight weeks under the supervision of a therapist. A summary of MBCT training sessions based on the Kabat-Zinn protocol has been presented in Table 1 (12). Data were analyzed using SPSS version 22 software.

Research instruments

A) Beck Depression Inventory (BDI-II): It is the revised Beck Depression Inventory which has been designed to assess the severity of depression in adults and adolescents aged 13 years and older and measures symptoms in the last two weeks. Convergent validity of the BDI-II was obtained with the Hamilton Rating Scale for Depression (HRSD) to be $r^2 = 0.71$. Accordingly, Cronbach's alpha of this questionnaire was 0.91, the test-retest reliability was 0.94 and the split-half reliability was 0.89 (13). In another study in Iran, its Cronbach's alpha coefficient was 0.87 and its test-retest reliability was obtained to be 0.74 (14).

B) Laboratory method and sampling: To measure serum cortisol, between 8 and 10 am in the morning, venous blood samples were taken from both control and experimental groups in two stages of pretest and posttest and were measured by luminescence method using the US Siemens Company Immulite device.

Table 1. Mindfulness-based cognitive therapy interventions (Crane, 2011)

Session	Topic	Summary of the session
First	Automatic guidance	Introduction to group members, explanation of the group rules, mindful eating exercise with a raisin, body checking meditation practice Task: Eating mindfully, bringing mindfulness to daily activities and body checking meditation
Second	Challenge with obstacles	10-minute mindful breathing and concentration, two ways to know, body checking practice and sitting meditation Task: Bringing mindfulness to daily activities, recording pleasant events, body checking practice and 10-minute mindful breathing
Third	Gathering the scattered mind Mindful breathing	Body stretching practice and mindful breathing, mindful movement meditation, 3-minute breathing space practice Task: Mindful movement meditation, a combination of body stretching and breathing meditation (days 1, 3, 5), recording unpleasant experiences, 3-minute breathing space practice
Fourth	Staying in the moment and avoidance detection	5-minutemindful seeing and hearing (awareness of breathing, body parts, sounds, thoughts and conscious choices), 3-minute breathing, providing modeled exercises for use in times of having difficult emotions (discovering unpleasant experiences and seeing negative thoughts), mindful walking Task: Sitting meditation (days 1, 3, 5), 3-minute breathing practice, mindful walking (days 2, 4, 6)
Fifth	Accepting and allowing	Sitting meditation practice with mindful breathing and awareness of body parts, practice of creating a problem and discovering the effects of the exercises on the mind and body, 3-minute pause practice (with a feeling of being receptive), the guest house metaphor Task: Sitting meditation(working with difficulties), 3-minute normal breathing and its review (three times a day), three minutes of practiced breathing in the session and modeling (for the time when you have unpleasant feelings: inviting a difficulty in and working with it through the body)
Sixth	Thoughts are not reality	Sitting meditation with a focus on thoughts as mental events Task: Body checking, 3-minute breathing space and using it in cases of unpleasant feelings by responding to the thoughts, "opening the doors of thought"
Seventh	Self-care	Continuous mindfulness practice, 3-minute breathing space, 3-minute responsive breathing space: In mindful action (doing enjoyable tasks and activities that feel being satisfied and useful), staying in the present Task: Preparing a list of enjoyable and useful activities
Eighth	Applying what you have learned and exercises in the future (now what?)	Performing formal and informal mindful exercises, 3-minute responsive breathing space, discussing the continuity of the exercises and planning to do them, cultivating a new way of being

Results

The results of the Shapiro-Wilk test revealed that the assumption of normal distribution of data in the variables of depression and cortisol is established in the experimental and control groups in the pre-test and post-test stages. Further, in the pre-test and post-test, the assumption of equal variances under the Levene's test is established in both groups ($P< 0.05$). Demographic findings indicated that in the experimental group, 30% were below diploma, 40% had a diploma and 30% had a bachelor's degree.

In the control group, 43.3% were below diploma, 20% had a diploma and 36.7% had a bachelor's degree. Furthermore, among the cancer and depressed patients in the experimental group, the mean ages were 29.93 years, and 32.87 years, respectively. In the control groups of cancer and depressed patients, the mean age was 32.53 years, and 33.93 years, respectively. Based on the results, 60% of the cases in the experimental group had minor depression, 36.7% had mild depression, and 3.3% had moderate depression. In the control group, 3.3% of them had minor depression, 3.6% had mild depression, and 93.3% had moderate depression. The results of Table 2 indicated that MBCT can be simultaneously effective in depression and serum cortisol levels in people with breast cancer and depressed people.

Table 2. The results of multivariate analysis of covariance and Wilks' Lambda test

Group	Source of effect	Wilks' Lambda	F statistic	DF	P	Effect size
Total	Pre-test depression	0.445	22.016	(3, 53)	<0.001	0.555
	Pre- test cortisol levels	0.277	46.082	(3, 53)	<0.001	0.723
	Treatment	0.027	636.749	(3, 53)	<0.001	0.973
Cancer group	Pre-test depression	0.495	7.824	(3, 23)	<0.001	0.505
	Pre-test cortisol levels	0.370	13.059	(3, 23)	<0.001	0.630
	Treatment	0.021	353.134	(3, 23)	<0.001	0.791
Depressed group	Pre-test depression	0.245	23.607	(3, 23)	<0.001	0.755
	Pre-test cortisol levels	0.238	24.582	(3, 23)	<0.001	0.762
	Treatment	0.021	350.939	(3, 23)	<0.001	0.907

With regard to the obtained effect size in the cancer group (0.791) and the depressed group (0.907), it can be stated that this effectiveness in the cancer group was less than the depressed group (Table 2). The results of the post-hoc test also indicated that the level of depression in the depressed group (10.13) improved more than the cancer group (13.27) after treatment ($P< 0.001$) (Table 3).

Table 4 presents the effectiveness of MBCT in cortisol levels in cancer patients and depressed individuals.

Table 3. Comparing the effectiveness of mindfulness-based cognitive therapy in depression among people with breast cancer and depressed people

Source of effect	Sum of squares	Degrees of freedom	Mean sum of squares	F Statistic	P
Pre-test	328.638	1	328.638	56.869	<0.001
Disease group	148.388	1	148.388	25.678	<0.001
Error	156.029	27	5.779		

Table 4. Comparing the effectiveness of mindfulness-based cognitive therapy in serum cortisol levels in people with breast cancer and depressed people

Source of effect	Sum of squares	Degrees of freedom	Mean sum of squares	F Statistic	P
Pre-test	68.281	1	68.281	5.854	0.023
Disease group	105.056	1	105.056	9.007	0.006
Error	314.933	27	11.664		

Given the effect size obtained in the cancer group (0.205) and the depressed group (0.295), it can be mentioned that this effectiveness in the cancer group was different from the depressed group. The results suggested that cortisol levels decreased in the depressed group after the intervention and increased in the cancer group (Table 5).

Table 5. Results of Bonferroni post-hoc test in comparing serum cortisol levels among people with breast cancer and depressed people

Variable	Group	Pre-test	Post-test	Adjusted mean in post-test	Mean difference	Standard error	P
Serum cortisol levels	Cancer	11.71	14.71	15.378	4.090	1.363	0.006
	Depressed	14.100	11.95	11.288			

Discussion

The results of this study demonstrated that the effect of MBCT on depression among breast cancer patients and depressed people was significant after adjusting the pre-testing effect. In other words, this treatment reduced depression among the two experimental groups. On the other hand, the study suggested that the depressed group showed more improvement in terms of the level of depression after treatment compared to the cancer group. This finding is consistent with the studies on mindfulness-based cognitive therapy conducted by Kenne Sarenmalm et al. (15) in people with breast cancer and the studies by Sedighi et al. (16), Norouzi (17), Sanada et al. (18), and Parmentier et al. (19) in depressed patients.

In Rahmanian et al. study, MBCT reduces the perceived stress and emotional processing of women with breast cancer and increases their psychological capital (20).

Zhang et al. suggested that MBSR is effective in improving physiological functioning, cognitive functioning, fatigue, emotional health, depression, stress, and distress in depressed patients (21). According to the finding obtained by Almeida et al., rumination is one of the key psychological mechanisms of Fear of Cancer Recurrence (FCR), so it is logical that MBCT be effective in reducing FCR because it considers rumination as the main focus of the intervention (22).

Schell et al. found that MBSR has a significant effect on anxiety, depression, fatigue, and sleep quality in breast cancer patients and probably leads to partial recovery in patients (23).

In explaining the effectiveness of the treatment in reducing depression, it can be stated that negative thoughts can lead to negative emotions and ultimately aggravate the symptoms of depression. Mindfulness, by focusing on presence in the moment, can be very helpful in improving the cognitive symptoms of depression. Thus, patients learn to develop a wider moment-by-moment awareness instead of rumination, and this awareness leads to early detection of patterns related to the return of thinking, feelings and bodily sensations. The individual also becomes more aware of his own physical symptoms and can identify stress and depression symptoms before being depressed (24). The results obtained by Ter Avest et al. suggest that MBCT may be more beneficial for people with earlier onset and higher levels of rumination and also for patients with lower quality of life (25). Also, Kuhnt et al. (26) and Hamer et al. (27) indicated that physical symptoms such as fatigue and pain impair social functioning and quality of life. Further, fatigue is one of the most pervasive concerns among cancer patients with a prevalence of 50% to 100%. It may be present before, during and even after cancer-related treatments. This may affect patients' daily activities and lead to emotional suppression and increased levels of stress and depression. In fact, FCR and fatigue are two common symptoms experienced by cancer survivors even after cancer treatment is completed (28,29).

The results of this study also revealed that the effect of MBCT on serum cortisol was significant among patients with cancer and depression after adjusting the pre-testing effect. According to the findings, cortisol levels decreased in the depressed group after the intervention and increased in the cancer group. Despite the fact that the cortisol level of the cancer group was lower than the depressed group in the pre-test, the two groups had different effectiveness after the treatment so that an increase in the cancer group and a decrease in the depressed group were observed, which confirms the difference between the two groups. Mirmohammadi et al. indicated that in women with breast cancer, MBSR therapy is significantly effective in the variables of depression, stress and cortisol regulation (30).

In the study conducted by Farhangi, MBCT enables women with breast cancer to recognize and regulate their emotions and increases their psychosocial functioning (31). In explaining this finding based on what Dhabhar et al. (6) have stated, chronic stress causes stress

hormone dysfunction in the body in the long run and thus prevents a return to the normal state. Over time, these hormones can lead to physiological changes and serious health problems. For example, chronic stress may result in higher- or lower-than-normal cortisol levels, both of which can have significant negative effects on health (32). Brown et al. also showed low plasma cortisol levels among recently diagnosed breast cancer patients with a history of depression or PTSD. A high prevalence of PTSD has been observed in women with breast cancer, and the symptoms of PTSD are specifically associated with a tendency to suppress emotions (33). These studies explain the low cortisol level among breast cancer patients, despite the increased self-report of negative emotions, including depression, during this research. Gold et al. (34) and Moica et al. (35), also indicated that people with MDD show different psychological and neurobiological responses to stressful life events and increased serum cortisol levels are strongly associated with MDD.

Further, the findings of Wayne et al. (36) and Luo et al. (37) confirm the use of MBCT to improve the symptoms of fatigue, pain, sleep problems, depression, anxiety, and quality of life. Although cancer patients are exposed to stressful life events, MBCT is defined as a technique in which one learns to focus attention in the present to become aware of the thoughts and feelings of the mind and to observe them in a non-judgmental way to achieve physical peace and mental balance, and this gives patients a sense of integrity and inner unity (38). Mindfulness-based interventions reduce stress by improving self-regulation and increasing neural flexibility, leading to health benefits (39). Mindfulness meditation can also balance the Hypothalamic-Pituitary-Adrenal (HPA) axis through changes in the autonomic nervous system by reducing sympathetic activity and activating the parasympathetic nervous system, which may explain the observed effect of MBIs on systolic blood pressure and body relaxation (40).

The limitation of the present study is that the main target population included women patients with breast cancer, and depressed women, which limit the generalization of the results to different ages and males. Also, serum cortisol levels were not evaluated during different hours of the day in both pre- and post-treatment samples.

It is recommended that hospital officials and managers, psychiatrists and psychologists provide psychological treatment to patients as a top priority in their training programs in addition to physical therapy in order to promote the physical and mental health of patients.

Conclusion

Based on the findings of the present research, it can be concluded that mindfulness-based cognitive therapy can reduce depression of patients with depression and breast cancer and can also be effective in neurobiological mechanisms in addition to improving psychological symptoms.

Acknowledgements

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