



Mindfulness-based cognitive therapy in Korean patients with systemic lupus erythematosus: A pilot study

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ABSTRACT

Background: and purpose: The stress and systemic lupus erythematosus (SLE) are intertwined and affecting each other. This pilot study evaluated the mindfulness-based cognitive therapy (MBCT) in Korean patients with SLE. **Materials and methods:** The Korean version of the Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), Satisfaction with Life Scale (SWLS), and Perceived Stress Scale (PSS) were evaluated for the effect of the MBCT in 25 patients.

Results: The BDI-II, BAI, SWLS, and PSS before the MBCT were 24.2 ± 10.6 , 19.1 ± 9.7 , 14.7 ± 6.5 , and 20.4 ± 3.8 , respectively. Eighteen patients completed the MBCT. After the MBCT, BDI-II, BAI, and PSS improved to 17.4 ± 13.0 ($p < 0.01$), 13.4 ± 7.7 ($p = 0.04$), and 17.9 ± 4.6 ($p = 0.04$), respectively. However, SWLS and SLE disease activity did not.

Conclusion: The MBCT could reduce the anxiety, depression, and stress but not SLE disease activity.

1. Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease involving various organs, such as skin, kidney, lung, and heart, and presents diverse clinical manifestations. Although the pathogenesis of SLE is not understood fully, a vulnerable genetic background causing autoimmunity and hormonal and environmental factors have been suggested to contribute to its pathogenesis. SLE is a chronic and incurable inflammatory disease. Therefore, appropriate strategies must be established to prevent clinical exacerbation and organ damage in the management of patients with SLE [1,2]. A study, which evaluated whether stress aggravates clinical symptoms in 26 patients with SLE and 12 patients with chronic discoid lupus [3], found that 74.1% of patients with lupus perceived worse clinical symptoms as related to daily stress but not to stressful life events. Conversely, the worsening of symptoms of SLE makes patients more depressed and stressful. A previous study evaluated the relationship between SLE disease activity, salivary stress hormones, and mental stress in Korean patients with SLE [4]. The Beck Depression Inventory (BDI) scores in patients with SLE were elevated in comparison with those of healthy controls (HC).

Moreover, the BDI scores were correlated with the SLE Disease Activity Index (SLEDAI) scores, and SLE patients with higher SLEDAI scores had higher baseline Perceived Stress Scale (PSS) scores. Therefore, these data showed that stress and SLE were intertwined and can be understood as affecting each other negatively.

The mindfulness-based cognitive therapy (MBCT) is a group-based clinical intervention program that was initially made as a relapse-prevention treatment for depression [5]. The MBCT integrates East Asian meditation practices and perspectives into Western psychological epistemology and practices. The goal of MBCT is to interrupt automatic processes that can trigger a depressive episode in individuals who have historically had depression and to teach the patients to focus less on reacting to incoming stimuli [6]. Recently, several clinical trials have shown that the MBCT improves psychological symptoms, such as anxiety and depression, and quality of life (QoL) in patients with rheumatic diseases, such as fibromyalgia, rheumatoid arthritis (RA), or SLE [7–10]. Only one study evaluated the efficacy of the MBCT on QoL and psychological symptoms in patients with SLE according to a randomized single-blind clinical trial [7]. Such study revealed a significant difference in QoL and psychological symptoms between the MBCT and

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control groups. However, few evidences on the efficacy of the MBCT on psychological symptoms and disease activity outcomes in SLE are available.

Therefore, this study evaluated the effectiveness of the MBCT-based stress reduction program, consisting of six sessions, on psychological symptoms by selecting those who experienced chronic stress among patients with SLE. Furthermore, we examined the effects of the MBCT intervention on SLE disease activity in Korean patients with SLE.

2. Materials and methods

2.1. Participants

This single arm study was evaluated as a pre-post comparison. Initially, the sample size was calculated based on a 5% α error and a power of 95% to see a difference equal to two standard deviations (SD) of mean psychological symptoms score between pre-and post-data. A sample size of 45 patients for goal was calculated. Forty two patients with SLE who complained of stressed condition, depression or anxiety agreed the simple survey and were screened using the Korean version of Brief Encounter Psychosocial Instrument (BEPSI-K) by three rheumatologists (CHS, HAK, JYJ) in an outpatient Lupus clinic. The BEPSI composed to self-administered questionnaire for assessing stress. Those with BEPSI-K average scores of more than 2.4 were enrolled [11]. When 6–8 patients were registered, the MBCT was started as a group. Finally, we enrolled 25 patients of them at the department of rheumatology in our hospital between August 2015 and August 2017. The power with the enrolled participants at that time was calculated to 80%. All patients met four or more of the American College of Rheumatology criteria for the diagnosis of SLE [12].

We reviewed patients' medical histories, glucocorticoid doses, and use of immunosuppressive agents, including hydroxychloroquine, methotrexate, azathioprine, and mycophenolate mofetil. Laboratory tests, including complete blood counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complement 3 and 4, and anti-double stranded DNA (anti-dsDNA) antibody, were conducted on all patients before and after the MBCT. Patients' disease activity was evaluated using the SLEDAI [13].

2.2. Measurement and assessments

The data for this study were collected through a questionnaire that included the Korean version of the BDI-II, Beck Anxiety Inventory (BAI), Satisfaction with Life Scale (SWLS), and PSS [14–17]. Korean version of BDI-II has been validated for both healthy and ill Korean populations [15]. The BDI-II was used to determine depression, and patients answered 21 items on a scale of 0–3 according to how they felt at the time. Higher scores mean higher levels of depression. Korean version of BAI has also been validated for both Korean patients and non-patients [16]. The BAI was used to determine anxiety, and the score system is similar to the BDI-II. Korean version of SWLS was assessed for satisfaction of life and showed adequate levels of reliability and validity [17]. Korean version of PSS has also been evaluated for both healthy and chronic ill Korean populations [14,18]. The PSS is used to measure stress with 14 items. Surveys were conducted before and after the program.

The MBCT program in this study was led by two trained psychiatrists (SMC and LS) who followed the MBCT manual. The program comprised two-hour sessions and homework for six weeks. The program was conducted in five separate groups, each of which composed of up to eight participants. The weekly components in Smith et al. were adopted in this study [19]. The components of the program included (1) an introduction on the MBCT; establishing orientation of the session and setting the rules, (2) identification of automatic thinking pattern; seeing thoughts as ideas about what is going on rather than as facts, (3) changing negative thinking and perception distortion, (4) finding core

beliefs and changing of distorted thoughts creating a different relationship with experiences, understating how to create and use acceptance, changing mood and thoughts, (5) finding productive coping; achieving full awareness of feelings and thoughts and accepting them, and (6) ways to take good care of oneself. The homework was designed to encourage participants to follow mindfulness techniques in their everyday life.

2.3. Statistical analysis

Categorical variables are expressed as frequencies with percentage and continuous variables, as mean \pm SD. The changes from pre-to post-MBCT were assessed by a paired *t*-test and the McNemar's test for continuous and categorical variables respectively. All statistical analyses were two-sided and performed using the SAS statistical software, version 9.4 (SAS Institute, Cary, NC, USA). A *p*-value less than 0.05 was considered statistically significant.

2.4. Ethics approval

Our study was conducted in accordance with the ethical principles of the Declaration of Helsinki and approved by the Institutional Review Board of our hospital (IRB No. MED-SUR-14-291). Informed consent was obtained from all patients.

3. Results

3.1. Clinical characteristics of the participants

Table 1 shows the clinical characteristics, laboratory findings, and medications of enrolled patients with SLE. Patients had a mean age of 42.0 ± 7.6 years and comprised 24 females (96%). Their main clinical symptoms included arthritis (44%), oral ulcer (32%), and nephritis (20%). The mean score on the SLEDAI was 4.6 ± 3.2 . The mean level

Table 1
Clinical characteristics of 25 patients with systemic lupus erythematosus (SLE).

	Mean \pm SD or N (%)
Age, years	42.0 \pm 7.6
Gender (female/male)	24 (96)/1 (4)
BDI-II	24.2 \pm 10.6
BAI	19.1 \pm 9.7
SWLS	14.7 \pm 6.5
PSS	20.4 \pm 3.8
White blood cell count, μ L	6636 \pm 3600
Hemoglobin, g/dL	12.7 \pm 1.7
Platelet, $\times 10^3/\mu$ L	259.0 \pm 99.8
ESR, mm/hr	15.5 \pm 12.1
CRP, mg/dL	0.20 \pm 0.34
Complement 3, mg/dL	94.5 \pm 28.6
Complement 4, mg/dL	22.4 \pm 10.1
Anti-dsDNA antibody, IU/mL	22.1 \pm 35.5
SLEDAI	4.6 \pm 3.2
Fever	1 (4)
Oral ulcer	8 (32)
Arthritis	11 (44)
Rash	3 (12)
Nephritis	5 (20)
Hydroxychloroquine	22 (88)
Methotrexate	2 (8)
Azathioprine	4 (16)
Mycophenolate mofetil	4 (16)
Glucocorticoid dose, mg/d ^a	2.9 \pm 2.7

BDI-II, Beck Depression Index-II; BAI, Beck Anxiety Index; SWLS, Satisfaction with Life Scale; PSS, Perceived Stress Scale; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; Anti-dsDNA, anti-double stranded DNA; SLEDAI, SLE Disease Activity Index.

^a Prednisone-equivalent.

Table 2

Psychological survey before and after a mindfulness-based cognitive therapy (MBCT) in patients with systemic lupus erythematosus.

Measures	Before the MBCT (n = 18)	After the MBCT (n = 18)	p-value ^a	1 st follow-up (n = 11)	2 nd follow-up (n = 12)
BEPSI	12.4 ± 3.8	11.0 ± 3.3	0.08		
BDI-II	24.6 ± 11.2	17.4 ± 13.0	< 0.01	17.3 ± 10.2	16.4 ± 8.8
BAI	18.2 ± 9.5	13.4 ± 7.7	0.04	13.3 ± 7.8	12.8 ± 5.8
SWLS	13.9 ± 6.4	15.4 ± 8.3	0.48		
PSS	20.4 ± 3.2	17.9 ± 4.6	0.04		

^a The paired *t*-test was performed to compare mean values of several psychological survey scores before and after the MBCT. The 1st follow-up was conducted after a month, and the 2nd, after two months of completing the MBCT. BEPSI, Brief Encounter Psychosocial Instrument; BDI-II, Beck Depression Index-II; BAI, Beck Anxiety Index; SWLS, Satisfaction with Life Scale; PSS, Perceived Stress Scale.

of anti-dsDNA was 22.1 ± 35.5 IU/mL. The glucocorticoid dose immediately before the MBCT was 2.9 ± 2.7 mg/d prednisolone-equivalent. The mean score on the BDI-II was 24.2 ± 10.6, and that on the BAI, 19.1 ± 9.7. The mean score on the SWLS was 14.7 ± 6.5, and that on the PSS, 20.4 ± 3.82.

3.2. MBCT and psychologic evaluations

Eighteen patients with SLE completed the MBCT program. After the MBCT, their mean score on the BDI-II improved to 17.4 ± 13.0 (*p* < 0.01), but that on the BAI fell to 13.4 ± 7.7 (*p* = 0.04). Their mean PSS score also improved to 17.9 ± 4.6 (*p* = 0.04). However, their mean SWLS score was not different between before and after the MBCT. When followed up for their BDI-II and BAI scores after two months, they obtained scores similar to those of immediately after the MBCT (Table 2).

3.3. MBCT and disease activities of SLE

We evaluated the effect of the MBCT on disease activity in patients with SLE. We found no difference in the laboratory findings and clinical manifestations between before and after the MBCT, except for arthritis (Table 3). Their medications also did not change after the MBCT. Likewise, their mean glucocorticoid dose was similar between before and after the MBCT.

4. Discussion

This study designed a single arm pilot study to evaluate whether the MBCT modifies psychological condition and disease activity in patients with SLE. In this study, we could compare improvement in depression, anxiety, and QoL only between before and after the MBCT. After the MBCT, their BDI-II, BAI, and PSS scores improved, of which the former two were maintained for two months. However, no significant difference in disease activity markers was found between before and after the MBCT.

Psychological therapies have been applied to reduce stress, anxiety, and physical complications in several studies for SLE [7,20,21]. A study evaluated the effects of a stress-reduction program on pain and physical or psychological function of 92 patients with SLE who experienced pain [20]. Such study's stress-reduction program involved a biofeedback-assisted cognitive-behavioral treatment (BF/CBT), was compared with a symptom-monitoring support intervention or usual medical care. The BF/CBT group significantly improved in pain and psychological dysfunction at a nine-month follow-up assessment. However, no change in the SLEDAI and Systemic Lupus Activity Measure-revised scores was observed. A similar result was obtained by another study on CBT [21], which demonstrated that a psychological intervention involving 10

Table 3

Clinical manifestations and laboratory findings before and after a mindfulness-based cognitive therapy (MBCT) in 18 patients with systemic lupus erythematosus (SLE).

	Before the MBCT Mean ± SD or N (%)	After the MBCT Mean ± SD or N (%)	p-value
White blood cell count,/ μL	5722 ± 2019	5325 ± 1946	0.22
Hemoglobin, g/dL	12.9 ± 1.8	12.5 ± 1.7	0.06
Platelet, x10 ³ /μL	242.1 ± 79.2	243.6 ± 87.7	0.51
ESR, mm/hr	14.0 ± 12.6	13.3 ± 13.2	0.92
CRP, mg/dL	0.2 ± 0.3	0.20 ± 0.35	0.76
Complement 3, mg/dL	93.2 ± 32.4	88.7 ± 35.0	0.22
Complement 4, mg/dL	22.6 ± 11.1	25.5 ± 23.4	0.49
Anti-dsDNA antibody, IU/mL	22.4 ± 36.8	24.9 ± 37.8	0.41
SLEDAI	4.3 ± 3.3	5.1 ± 2.9	0.19
Fever	1 (5.6)	0 (0)	N/A
Oral ulcer	5 (27.8)	4 (22.2)	0.56
Arthritis	7 (38.9)	11 (61.1)	0.05
Rash	3 (16.7)	3 (16.7)	N/A
Nephritis	3 (16.7)	3 (16.7)	N/A
Hydroxychloroquine	15 (83.3)	15 (83.3)	N/A
Methotrexate	2 (11.1)	2 (11.1)	N/A
Azathioprine	4 (22.2)	4 (22.2)	N/A
Mycophenolate mofetil	2 (11.1)	2 (11.1)	N/A
Glucocorticoid dose, mg/ ^a	2.7 ± 2.7	3.0 ± 3.0	0.35

The data of before and after the MBCT were assessed using the paired *t*-test and the McNemar's test for continuous and categorical variables, respectively. N/A is not assessed because a statistical test cannot be computed due to insufficient cell size. ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; Anti-dsDNA, anti-double stranded DNA; SLEDAI, SLE Disease Activity Index.

^a Prednisone-equivalent.

sessions of CBT improved anxiety, stress, depression, and QoL but did not improve disease activity in patients with SLE. Only one study evaluated the effectiveness of the MBCT on psychological symptoms and QoL in 46 patients with SLE [7]. They conducted a randomized single-blind clinical study in patients with SLE and assigned them into the MBCT and control groups in which the former underwent eight sessions of the MBCT program. Compared with the control group, they found a significant improvement in psychological symptoms and QoL immediately after all the sessions and at follow-up in the MBCT group, but no difference in physical components of QoL between the groups. However, they did not evaluate the effect of the MBCT on SLE disease activity. Patients' baseline laboratory findings and clinical manifestations were also not revealed. Although the present study is single arm, patients were followed up for two months after completing all six sessions of the MBCT. Their depression, anxiety, and stress levels improved immediately after the sessions. Their depression and anxiety levels were also maintained during the follow-up period. However, patients' QoL and disease activity did not improve after the MBCT. These results were similar to the previous studies for effect of psychological components on the MBCT or BF/CBT [7,20]. Although the MBCT is expected to be effective in controlling disease activity of SLE, the results of this study did not confirm such hypothesis, similar to previous studies [20,21]. However, the duration of the MBCT in this study could be relatively short, which resulted in the lack of impact on disease activity of SLE. There have been few studies with MBCT or BF/CBT to improve disease activity in patients with SLE, but there were some reports in other chronic inflammatory disorders [9,22]. One study revealed that mindfulness-based stress reduction (MBSR) impacted RA disease activity, such as joint tenderness, global assessment, and pain [9]. Their MBSR group received an eight-week program; follow-up assessments were conducted at two, four, and six months. In patients with inactive ulcerative colitis, a randomized controlled trial of MBSR was evaluated to prevent flare-ups [22]. Although MBSR did not affect the rate or

severity of flare-ups in patients with ulcerative colitis, it was effective in improving QoL especially for patients with high stress reactivity during remission. Therefore, it cannot be concluded that the MBCT is not effective on SLE disease activity. A larger study with double arm and long-term follow-up would be needed.

The effect of MBCT on psychological component of the patients with SLE could be explained to this intervention's unique mind-body combination, which is associated to the patients with SLE. There was an evidence that cortisol levels, known as a stress hormone, decreased following participation in an MBSR program [23]. Furthermore, several studies showed the positive effects of meditation on brain function and left-sided prefrontal activity, which has been associated with immune function [24–26]. Therefore, the MBCT may be effective for psychological improvement in patients with SLE. However, this study was limited by its small sample size with power of 80% and single-arm design. Furthermore, about 30% of the patients were also not followed up during this trial. We deemed that visiting the hospital weekly is taxing for patients, especially the depressed ones.

5. Conclusion

This pilot study provided preliminary evidence on the use of the MBCT in reducing anxiety, depression, and stress in patients with SLE but not SLE disease activity. Because this study had a relatively short-term intervention with a short follow-up period, future study on MBCT must involve a long-term intervention with a multicenter large cohort.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Authorship

All authors have materially contributed to the conception and design of the study and interpretation of data, drafting of the article and have approved the final article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ctcp.2019.01.009>.

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