

Effectiveness of Mindfulness Based Cognitive Therapy on the Quality of Life, Depression and Burden of Demented Women Caregivers

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Article information	Abstract
<p>Article history: Received: 23 June 2012 Accepted: 18 July 2012 Available online: 9 Jan 2013 ZJRMS 2014 Sep; 16(9): 5-11</p> <p>Keywords: Mindfulness based cognitive therapy Quality of life Depression Burden Demented woman Caregiver</p> <p>*Corresponding author at: Department of Psychology, Faculty of Psychology, Allameh-Tabatabaee University, Tehran, Iran. E-mail: mercede1988@gmail.com</p>	<p>Background: The aim of the study was to observe whether the Mindfulness Based Cognitive Therapy (MBCT) is effective in easing the life burdens, alleviating mental depression and also improving the quality of life of female caregivers of Alzheimer's patients.</p> <p>Materials and Methods: In this investigation, the quasi-experimental method was used. In this research, statistical society is women caregivers that they are members of Alzheimer's association. For this purpose, 20 of the women caregivers of Iranian Alzheimer's association, 10 of experimental group and 10 of control group, were selected. The methods of sampling were according to the type of available samples and were placed randomly in the two groups of experimental and control subjects. Eight therapy sessions were held and these two groups were asked by the researchers to respond to the Quality of Life questionnaire (SF-36), Burden of Care Givers questionnaire (CBI) and Hamilton questionnaire. These replies were gathered by researches once before the beginning of each session, once at the end of each therapy session and also once 2 months after the end of the therapy was completed. For analyzing has been used SPSS-16. The Covariance test and Wilcoxon test were used to analyze the gathered data.</p> <p>Results: The observed findings in the 2-month follow ups show that this therapy has long term effects on depression and easing the burden of life, but it has minimal to no long term effect on the improvement of the quality of lives of study subjects.</p> <p>Conclusion: The results indicate that (MBCT) is, in fact, effective in improving the quality of life and reducing the depression and burden of lives of the female caregivers of Alzheimer's patients.</p>

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Introduction

A family caregiver is a person whom voluntarily takes care of another family member who is afflicted with some health disorder, but is not capable of looking after him or herself [1]. Taking care of these patients would lead to depression and a decrease in the physical health of the caregiver [2]. Burden of the caregivers is a concept which studies the negative effects of care giving on physical and mental wellbeing of the caregivers which, in turn, can influence the caregivers' work, finances and social lives in a negative manner [3]. The labeling someone as a caregiver could lead to an increase in his/her life hardships. Therefore, mental intervention therapies should be used in order to decrease the effects of such burden levels [4]. Some of the main problems of the caregivers are depression disorders. These disorders can be recognized by the presence of symptoms such as severe sadness, inability to experience joy for more than two weeks at a time, inability or decrease in quality of sleep, loss of appetite, decrease in maintaining attention, the feeling of worthlessness, lethargy and an inclination toward suicide [5]. Quality of life as defined by the World Health Organization is "the perception of the individual of his position in life in the context of culture and value system in which he lives and

in relation to his objectives, expectations, patterns, and worries" [6]. In a research with the subject of the relationship between depression and the life quality of the dementia patients' caregivers, it was shown that there is a direct relationship between the increase in the risk of depression with the increase of responsibility levels while a decrease in the scales of life quality in physical and psychological domains exists. In addition, it was observed that an increase in the quality of lives of the caregivers, would lead to providing a better quality of care for their patients [7]. Mindfulness based cognitive therapy of caregivers, and training of mental techniques such as the control of emotions at times of stress, are useful tools to be used by therapists on clinical and non-clinical populations. Mindfulness based cognitive therapy has been developed by cognitive researchers for preventing depression and its recurrence [8]. Heeringen and Godfrin have found the positive effects of Mindfulness based cognitive therapy on periods of depression, mental health and life quality [9, 10]. Used MBCT to decrease the stress levels on 78 caregivers of Alzheimer's patients with significant positive results and so far other therapies and techniques have not had this amount of responsiveness [10]. The study of Pattayanak [11] indicates that female

caregivers, especially from Asian nations, have higher levels of burden. These findings are consistent with the study done by Prasad and Rani where they reasons that such increases in stress levels and negative mental status could be because of the fact that women in Asian nations have to negotiate the extra “duties” of more demanding spouses, upbringing of higher number of children and the societal expectation of providing care to the older members of the family [12].

Materials and Methods

In research statistical society is women caregivers that they are members of Alzheimer's association. In order to compare the results and to measure the effects of any independent variable, our samples included one experimental group and one control group. Research samples were obtained from Alzheimer's caregivers who were the members of Alzheimer association. The selection of sampling method was based on the type of sampling available through membership and referring of Alzheimer association. The volume of sample was 20 individuals which consisted of 10 participants in the experimental group and another 10 in the control group. The referred partakers who were diagnosed with depression, decrease quality of life and low burden according to the tests, were allocated randomly to these two groups. Instruments involved:

1. Hamilton's ranking scale of depression: This scale has been developed by Max Hamilton for measuring the amount of depression [13]. Summarize the results from studies examining internal reliability and validity was described in Bagby [14].

2. Quality of life SF-36 questionnaire: Mental and physical health questionnaire SF-36(V2) Ware 1996: this 36-question questionnaire measures mental and physical health through 8 scales (physical function, physical role, body pain, general health, liveliness, social function, excitation role, and mental health) [15]. Fooladvand et al., research about reliability case of this questionnaire in Iran [16].

3. Caregiver Burden Inventory (CBI): The responsibility of caregivers is measured by the questionnaire of caregivers' responsibility (CBI). This questionnaire has been developed by Nowak Wegest in 1988 reliability and validity was described in Caserta research [17]. For estimating the validity coefficient regarding the scale of the measuring of the burden of the caregivers, due to the fact that questions have multi values (not at all, a little, medium, relatively and completely) the Cronbach's Alpha has been used. Due to the gained coefficient of Alpha in the scale of measuring the burden of caregivers (CBI) equal to 0.86 we can conclude that this scale has a rather high reliability coefficient.

In this investigation, the quasi- experimental method was used as the research method. The group under the mindfulness based cognitive therapy had 8 weekly sessions of 2.5-hour periods. The first session consisted of the introduction and acquaintance of members and the leader of the group. Also, the primary principles and the

aim of the work were discussed and the members were asked for their ideas. Each of the later sessions included teaching the techniques in theory and as hands on exercises and evaluation of tasks. After that an assignment was provided to the group for further discussion and also recording of the results of the exercises were done. In each session, in addition to teaching the new technique of exercising the tasks, the previous techniques were reiterated and the impediments and possible solutions were also discussed. Eventually, after the end of 8 sessions, the questionnaires were presented and the value and the degree of variance of the variables of the research were compared. Two months after the end of the eighth sessions, another session was held and the tests were re-conducted later, this intervention were used for control group (waiting group). Data analyses: Due to the fact that the hypotheses were all already established, along with the inferential analysis and testing of the research, the covariance tests were also used. The covariance test and Wilcoxon test were used to analyze the gathered data for analysing has been used SPSS-16 and $p \leq 0.05$ was considered as significant difference.

Results

Indicators of descriptive statistics related to quality of life, depression, burden off female caregivers of Alzheimer's patients of Tehran, Iran has been estimated separately. Descriptive data of each variable has been presented in table 1. The descriptive statistics of pretest and post test grades regarding quality of life, depression and burden of caregivers has been presented separately for each of the groups. According to the results of this table, the mean of the pretest grades of the quality of life of the experimental group is 58.01 and in control group is 47.61. Also the mean of the grades of the experimental group in post-test is 70.98 and in controlled group 37.57 and in follow-up stage the grade s of the experimental group is 68.93. Considering the above results, the mean score of quality of life of the experimental in post-test and follow up has been increased which indicates a better quality life after the therapy. But in the controlled group the mean of quality of life score has been decreased. Regarding the scores of depression as we can see in table 1 also, the mean score of pre-test of the experimental group is 20 and in the controlled group is 12.7. Also, the mean score of the experimental group in post-test is 6.7 and in controlled group is 19.4 and in follow up the score of experimental group is 4.2. Considering the above results, the mean score of depression of the experimental group in post-test and follow up test has been decreased. But in the controlled group the mean score of the depression has increased. Regarding the scores of “burden of caregivers” also the mean score of pre-test of experimental group is 31.6 and in controlled group is 25.3. Also the mean score of experimental group in pre-test is 24 and in controlled group is 44.7 and in follow up test the score of experimental group is 17.6. Due to the above gained results, the mean score of “burden of

caregivers” of experimental group in post-test and follow up has been decreased which indicate the better burden of them but in the controlled group the mean score has been increased. In order to better descriptive of means of experimental and control groups is displayed separated. Bar Graphs for each of groups. Before analyzing the related data to the hypotheses, for making sure that these data would provide the infrastructures of the hypothesis of the covariance analysis, we will evaluate them. For this purpose four assumptions of covariance analysis including normality, linearity, homogeneity of variance and homogeneity of regression were tested, which are described respectively.

One of the important assumptions for covariance analysis is the normality of distribution of the dependant variable in each group. For evaluating this assumption, we have used the Kolmogorov-Smirnov test, results of Kolmogorov-Smirnov test for evaluation of the normality of distribution of scores of “quality of life, depression, burden” is presented the score distribution in the two groups “quality of life, depression, burden” in the level of 95% ($\alpha=0.05$) are not significant. In other words, due to the fact that the mentioned test is not significant, it means that the zero assumption for normality of distribution of scores of quality of life, depression, burden in both of the groups is confirmed. And with a certainty of 95% we can conclude that the distribution of the scores of quality of life in both the groups is normal. One of the pre-assumptions tests analyses of covariance is homogeneity of variance in both the groups. Before providing the research hypothesis and testing it, for determining that whether the homogeneity of variance has been considered in both the groups or not, the Levine test was performed. The results of Levine test for evaluating the homogeneity of variance has been presented. The homogeneity of variance of both of the groups in scores of “quality of life, depression, burden” are in the level of 95% ($\alpha=0.05$) and are not significant. In other words, due to the fact that the insignificance of Levine test, means that the zero assumption of the homogeneity of variance in both the groups are confirmed, with a certainty of 95% we can conclude that the variances of both groups in scores of “quality of life, depression, burden” are similar. Homogeneity of the slope of the regression line is another one of the assumptions of this analysis. This should be assumed that the regression lines for each group of the research should be equal and similar. If the regression is not homogeneous, the covariance will not be a proper analysis. Assuming that the slope of the regression line is homogenous is one of the key issues in covariance. The gained results from this analysis has been presented in the below. The results of the analysis of the homogeneity of the slope of the regression line as a pre-assumption of the covariance analysis has been provided. The level of significance of mutual effect (group quality of life, depression, burden) are greater than $\alpha=0.05$ and, therefore, the assumption of the homogeneity of the slope of the regression line are accepted. In table 2 the results of covariance analysis of post-test with removing the effect

of pre-test between the two groups has been presented. According to the results of the table, since the calculated F value (37.42) with freeness degrees of 1 and 17 is greater than the F value of the table (8.40) and due to the obtained significance level which is less than ($\alpha=0.01$) the null assumption (zero) is rejected and the hypothesis 1 is confirmed with a level of 99% certainty. According to the results of table 1, the mean score of post-test in experimental group has been increased comparing to the controlled group, which is a significant difference. The obtained effect indicator, indicate that 68% of the increase in quality of life of the participants can be related to the “mindfulness based on cognitive therapy”. The statistical power is equal to 0.997. In other words, if the same survey (research) will be repeated for 1000 times the probability that the null assumption would be confirmed is only 3 times. Hypothesis 2: Mindfulness based on cognitive therapy has effect on “depression” of Alzheimer's women caregivers. For testing this hypothesis, due to the fact that all the assumptions of covariance analysis are established, we have used this test and the results are presented in table 3. In table 3 the results of covariance analysis of post-test with removing the effect of pre-test between the two groups has been presented.

According to the results of the table, since the calculated F value (19.66) with freeness degrees of 1 and 17 is greater than the F value of the table (8.40) and due to the obtained significance level which is less than ($\alpha=0.01$) the null assumption (zero) is rejected and the hypothesis 2 is confirmed with a level of 99% certainty. According to the results of table 1-4, the mean score of post-test in experimental group has been increased comparing to the controlled group, which is a significant difference. The obtained effect indicator, indicate that 53% of the decrease in “depression” of the participants can be related to the “mindfulness based on cognitive therapy”. The statistical power is equal to 0.98. In other words, if the same survey (research) will be repeated for 100 times the probability that the null assumption would be confirmed is only 2 times. Hypothesis 3: Mindfulness based on cognitive therapy has effect on burden of Alzheimer's women caregivers. For testing this hypothesis, due to the fact that all the assumptions of covariance analysis are established, we have used this test and the results are presented in table 4. In table 4 the results of covariance analysis of post-test with removing the effect of pre-test between the two groups has been presented. According to the results of the table, since the calculated F value (15.63) with freeness degrees of 1 and 17 is greater than the F value of the table (8.40) and due to the obtained significance level which is less than ($\alpha=0.01$) the null assumption (zero) is rejected and the hypothesis 3 is confirmed with a level of 99% certainty. According to the results of table 1, the mean score of post-test in experimental group has been increased comparing to the controlled group, which is a significant difference. The obtained effect indicator, indicate that 53% of the decrease in burden of the participants can be related to the

"mindfulness based on cognitive therapy". The statistical power is equal to 0.96. In other words, if the same survey (research) will be repeated for 100 times the probability that the null assumption would be confirmed is only 4 times. Hypothesis 4: the effect of mindfulness based on cognitive therapy on the level of "quality life" of the Alzheimer's women caregivers, during the 2 months follow-up period is continuous. For evaluating this hypothesis, due to the small size of the sample ($N < 30$), abnormality of the scores distribution and disability to establish the pre-assumptions, the parametric Wilkackson test has been used. This test is one of the strongest and non-parametric tests and is one of the most useful replacement for *t*-test when dealing with two dependant groups. The results of this test are presented in table 5. According to table 5, 2 months after implementing the mindfulness based on cognitive therapy, "the quality of life" has been decreased in 3 and increased in the rest 7 person of the group. Also, considering the absolute calculated Z value is equal to 1.476 and is less than 1.96, therefore, it can be concluded that there is no difference in significance of "quality of life" in pre-test and after 2 months follow-up period. So, the null assumption is confirmed and it can be concluded that the mindfulness based on cognitive therapy doesn't have the necessary effect on the "quality of life" of the Alzheimer's women caregivers. Hypothesis 5: the effect of mindfulness based on cognitive therapy on the level of "depression" of the Alzheimer's women caregivers, during the 2 months follow-up period is continuous. For evaluating this hypothesis, Wilkackson test has been used. The results of

this test are presented in table 6. According to table 6, 2 months after implementing the mindfulness based on cognitive therapy, "depression" has been decreased in all the 10 persons of the group. Also, considering the absolute calculated Z value is equal to 2.809 and is less than 2.58, therefore the level of significance is more than 0.01 and we can say that there is a significant difference in "depression" in pre-test and after 2 months follow-up period with a level of certainty of 99%. So, the null assumption is confirmed and it can be concluded that the mindfulness based on cognitive therapy has a positive effect on the "depression" of the Alzheimer's women caregivers. Hypothesis 6: the effect of mindfulness based on cognitive therapy on the level of "burden" of the Alzheimer's women caregivers, during the 2 months follow-up period is continuous. For evaluating this hypothesis, Wilkackson test has been used. The results of this test are presented in table 7. According to table 7, 2 months after implementing the mindfulness based on cognitive therapy, "burden" has been decreased in all the 10 persons of the group, which indicate a better tolerance among them. Also, considering the absolute calculated Z value is equal to 2.805 and is more than 2.58, therefore the level of significance is less than 0.01 and we can say that there is a significant difference in "tolerance" in pre-test and after 2 months follow-up period with a level of certainty of 99%. So, the null assumption is confirmed and it can be concluded that the mindfulness based on cognitive therapy has a positive effect on the "tolerance" of the Alzheimer's women caregivers.

Table 1. The mean and deviation of indicators of quality of life, depression, burden of caregivers in experimental group and controlled group in pre-test, post-test and follow up stages

Variable	Stage	Group	Statistical indicator		
			Number	Mean	Deviation
Quality of life	Pre-test	Experimental group	10	58.01	24.01
		Controlled group	10	47.61	18.32
	Post-test	Experimental group	10	70.98	11.11
		Controlled group	10	37.57	12.80
	Follow-up	Experimental group	10	68.93	18.3
		Controlled group	-	-	-
Depression	Pre-test	Experimental group	10	20	6.16
		Controlled group	10	12.7	4.57
	Post-test	Experimental group	10	6.7	2.54
		Controlled group	10	19.4	9.21
	Follow up	Experimental group	10	4.20	3.64
		Controlled group	-	-	-
Burden of the caregiver	Pre-test	Experimental group	10	31.60	16.36
		Controlled group	10	25.30	7.33
	Post-test	Experimental group	10	24	14.25
		Controlled group	10	44.7	13.71
	Follow-up	Experimental group	10	17.6	17.46
		Controlled group	-	-	-

Table 2. Results of covariance analysis of the adjusted mean difference of the scores of the effect of mindfulness based on cognitive therapy on quality of life of the Alzheimer's women caregivers in experimental and controlled groups

Sources of change	Sum of squares	Freeness degree	Mean of squares	F ratio	Significance	Square of Ata	Statistical power
Pre-test	591.08	1	591.08	5.03	0.03	0.228	0.562
Groups	4397.54	1	4397.54	37.42	0.001	0.688	0.997
Error variance	1997.43	17	117.46	-	-	-	-
Total	67095.22	20	-	-	-	-	-

Table 3. Results of covariance analysis of the adjusted mean difference of the scores of the effect of mindfulness based on cognitive therapy on "depression" of the Alzheimer's women caregivers in experimental and controlled groups

Sources of change	Sum of squares	Freeness degree	Mean of squares	F ratio	Significance	Square of Ata	Statistical power
Pre-test	99.09	1	99.09	2.32	0.145	0.12	0.30
Groups	836.6	1	836.6	19.66	0.001	0.53	0.98
Error variance	723.4	17	42.55	-	-	-	-
Total	20	20	-	-	-	-	-

Table 4. Results of covariance analysis of the adjusted mean difference of the scores of the effect of mindfulness based on cognitive therapy on burden of the Alzheimer's women caregivers in experimental and controlled groups

Sources of change	Sum of squares	Freeness degree	Mean of squares	F ratio	Significance	Square of Ata	Statistical power
Pre-test	659.75	1	659.75	3.92	0.06	0.187	0.463
Groups	2629.97	1	2629.97	15.63	0.001	0.479	0.96
Error variance	2860.35	17	168.25	-	-	-	-
Total	20	20	-	-	-	-	-

Table 5. Results of Wilkackson test regarding the comparison of pr-test and post-test scores of quality of life in experimental and controlled groups

Variable	Level	Number	Mean of ranks	Sum of ranks	Z statistics	Significance level
Pre-test, follow up of "quality of life"	Negative levels	3	4.33	13	-1.478	0.139
	Positive levels	7	6	42		
	Constant levels	0	-	-		
	Total	10	-	-		

Table 6. Results of Wilkackson test regarding the comparison of pr-test and post-test scores of "depression" in experimental and controlled groups

Variable	Level	Number	Mean of ranks	Sum of ranks	Z statistics	Significance level
Pre-test, follow up of "quality of life"	Negative levels	10	5.5	55	-2.809	0.005
	Positive levels	0	0	0		
	Constant levels	0	-	-		
	Total	10	-	-		

Table 7. Results of Wilkackson test regarding the comparison of pr-test and post-test scores of "burden" in experimental and controlled groups

Variable	Level	Number	Mean of ranks	Sum of ranks	Z statistics	Significance level
Pre-test, follow up of "quality of life"	Negative levels	10	5.5	55	-2.850	0.005
	Positive levels	0	0	0		
	Constant levels	0	-	-		
	Total	10	-	-		

Discussion

It is evident from the research findings that the cognitive therapy based mindfulness improved Alzheimer caregiver's quality of life. Statistical result showed that this treatment improved Alzheimer caregiver's quality of life up to 68%. Therefore, the hypothesis was confirmed based on findings. Takai reviewed caregiver's quality of life found that they have physical, social and particularly psychological problems. Also, Takai showed that the caregiver's quality of life affects caring for patient, thus the quality of life is a top priority for the caregiver [7]. Moreover, this type of mental health reduces other mental incapacities. Cognitive therapy based mindfulness, by accepting experiences and being impartial relative to events, prevents a person to get engaged in the thought-emotion vicious circle when facing stressful incidents and thus avoid consequent negative assessments and intellectual pondering. Also, this therapy makes use of practical techniques to create self-awareness of body's physical situation to increase attention towards physical

health. Respiration/meditation techniques lead to more concentration and mental focus and therefore, prevent spontaneous thoughts and negative emotions. So, cognitive therapy based mindfulness actually improves quality of life by pushing up body and mind which are 2 basic components of quality of life. Another finding of cognitive therapy based mindfulness may reduce caregiver's depression. The research results showed this treatment can reduce depression symptoms down to 53% and confirmed this hypothesis. Gatrfin and Haringen found positive effect of treatment based on cognitive therapy based mindfulness on depression cycles, mental health and quality of life. Hypothesis findings were in line with the research [9]. Razande studies confined that the Alzheimer caregivers were prone to anxiety, depression, physical illness and low self-confidence and depression affects their lifestyle and isolates them against social conduct [18]. Main function of cognitive therapy based mindfulness affects thought process and is used to prevent recurring depression. This treatment breaks open the thought-emotion vicious circle and prevents consequent negative assessments and

intellectual pondering and when the going gets tough, it teaches the individual how to maintain focus, awareness of present time, impartiality, and responsiveness based on holistic situation. Therefore, it prevents augmentation of thought-emotion vicious circle and establishes a positive feedback loop between negative emotion and negative thought patterns. So, although stress-initiated communications network includes negative cognition/emotions, but metal techniques may change this vicious circle [8, 19] it ultimately reduces depression. In fact, depressive people, by stressing on more awareness of affairs and automated guidance, would learn to become more aware of the primary symptoms list of depression warning. Their practice makes the job perfect. It is a program based on body investigation exercise. In the next sessions, breathing/body meditation, and sound and light techniques are introduced. Yoga exercises and mental focus treatment help draw the attention to bodily senses which are common in most depression psychological treatments. MBCT program, makes use of a mental-educational model. Stress relieving techniques like concentration on breathing or Yoga are usually the people's choice for improving health in leisure time. However, besides that the participants are thought that by expanding their attention every moment, they may perform better in monitoring their thoughts, emotions and senses.

Further findings showed that MBCT may reduce caregiver's burden. Research result showed that the MBCT reduced caregiver's burden down to 53%. The lower burden ameliorates other mental problems and enhances mental health. Shang found that there is in fact a relationship between caregiver's burden and mental/physical health. Stressors reduce joyful or normal caregiver activities and ends in depression [20]. Also, the enhancement of quality of life for Alzheimer patients' female caregivers in a 2-month phase continues. Research showed some improvement by using this treatment to enhance quality of life for Alzheimer patients' female caregivers in a 2-month phase. The reason could be that the quality of life component includes physical, mental and social health which is a multidisciplinary concept, thus the changes in this component may take place by changing all its aspects through continuing treatment sessions and exercises in the long run. The reason for instability of this treatment for quality of life may also point to the fact that the quality of life changes during treatment and the individual's interpretation of life may

change accordingly and thus, people's quality of life may undergo changes. Another finding showed that the effect of MBCT continued to reduce depression of Alzheimer patients' female caregivers in a 2-month phase. Results showed that this treatment has been effective even 2 months after the end of treatment. People who accepted practical techniques of this therapy and included them in their daily life experienced lower depression levels and avoided its recurrence, so the hypothesis result is confined. The last finding showed that the effect of MBCT continued to reduce burden of Alzheimer patients' female caregivers in a 2-month phase. Results showed that this treatment has been effective even 2 months after the end of treatment. The hypothesis result also confirms the continuing effect of this therapy to reduce patient's burden. Based on lower depression and continuing effects and the relationship of burden with depression, this result expressed the relationship of these 2 components and the effectiveness of cognitive therapy based mindfulness treatment for depression and burden.

One of the limitations of this research is the small size of its sample and another one is about the gender variable, since the sample is only consisted of women and considering the effect of this therapy in the 3 mentioned domain. In a nutshell, the research findings showed that the treatment has been effective on 3 components of a caregiver: quality of life, depression and burden. Since this ailment is spreading and caregiver's responsibilities are expanding which may lead to mental disorder and reduce mental health based on results of above research, continuous intervention for the caregivers, especially mindfulness intervention for its practical techniques which can be utilized outside treatment sessions, may be used for battement of caregivers.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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