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Efficacy of Stress Management Intervention on Psychological, Immune Factors and Pain in Rheumatoid Arthritis Patients

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Abstract

Objective: In this survey, the intervention of cognitive behavioral stress management (CBSM) on psychological and immune indices and pain in patients with Rheumatoid Arthritis is studied.
Method: Statistical population of the study consisted of patients who referred to the rheumatology clinics in the northern parts of Tehran. 44 participants aged 25–60 using purposive sampling in accordance with inclusion and exclusion criteria selected and in two groups of 22 individuals were examined. Psychological, immune and pain evaluation tests of depression, anxiety and stress scale, blood sample, and McGill pain inventory were conducted in two stages of pretest and posttest using multiple covariance analysis.
Results: The results showed a significant effect of the stress management intervention on depression ($F_{1,37}$= 4/318, P= 0/046, η^2 =0/104) among patients with RA. The use of this intervention was effective in reducing the immune parameter (CRP) ($F_{1,38}$= 17/593, P= 0/001, η^2 =0/316) and their pain ($F_{1,39}$= 4/885, P= 0/033, η^2 =0/111).
Conclusion: According to the results, employing this method for RA patients is very helpful and it can be suggested for improving their psychological and physical conditions.

Keywords: CBSM[1], psychological indices, ESR[2], CRP[3], rheumatoid arthritis.

Introduction

Healthy immune system is able to recognize self and non-self cellular components. The stimulating factors can disrupt immune system of human in an unsuitable genetic context so that the self cells of body (cells and their components) can be regarded non-self against the immune system of the body and react against it. These diseases are called autoimmune diseases. Rheumatoid arthritis is the common autoimmune disease which engages different organs including joint, kidney, blood, brain, heart and lung (Alishiri., 2012). The common symptoms of this disease include pain, inflammation, dryness and heat around joint, loss of appetite, weight loss, dry eye syndrome, dry mouth, and reduced movement of the damaged joints. Of course, the internal organs of body may be affected by it (Fauci., 2008; Zare & Khatavi., 2008). Rheumatoid arthritis has afflicted 0.5 to 1% of the global population (Imran, Anwer Khan, Mir Ahmad, Raja, Saeed, Haider., 2015).

All chronic painful diseases cause stress for their patients and their families and this stress becomes worse when it has severe and consecutive pain. In the case when the patients with Rheumatoid

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1- Cognitive behavioral stress management
2- Erythrocyte sedimentation rate
3- Creactive protein

arthritis become crippled, their condition is highly stressful for them and their families (Sarafino., 1940; Garmaroodi & Eftekhar Aerdabili, 2008).

Depression and anxiety are effective in aggravation of the clinical outcomes of Rheumatoid arthritis which includes two psychological and biological sections (Muscatell et al., 2014). One of the problems of common mental health among the adults with RA is depression (Morf, Malysheva & Baerwald; 2012; Kelly, Kelly & Hootman, 2015). Incidence of depression in the study by Morf et al., (2013) indicates the presence of depression in 34% of the patients. It was specified in this study that there is significant relationship between medium activity of disease, depression, pain severity, and the perceived stress. Depression is the main disorder and generalized anxiety is one of the ordinary psychiatric diagnoses among patients with RA (Chinglok et al., 2010). In fact, it is highly important to pay attention to psychological modes due to involvement with immunological factors in these diseases so that among the immune cells, condition of cytokines is very different in the depressed persons compared to the healthy persons (Lu, Mok, Cheng, Chi Cheng, Peng, Wang, et al., 2013). On the other hand, stress and incidence of the traumatic events is one of the factors causing central nerves system diseases and as they are regarded as organic system (Iwata, Ota & Duman, 2013), anxiety is also related to higher level of CRP, IL6, and TNF. Among the patients with Rheumatoid arthritis, chronic personal stress is more related to IL6 production. One of the major symptoms which accompanies patients with Rheumatoid arthritis and about which the patients complain is feeling of pain. This feeling is related to other mental and physical variables so that depression and anxiety can predict the current pain rate of the patients with RA (Smith & Zautra., 2008). These variables are related to each other so that depression acts as a moderating variable regarding effects of pain on sleeping disorder in these patients (Nicassio, Ormseth, Kay, Custodio, Irwin, Olmstead, Weisman., 2012). Some researchers believe that regulation of positive and negative emotion is a key variable for understanding experience of pain among the patients with Rheumatoid arthritis. On this basis, some interventions can be mentioned in this regard to take some actions for improvement of medical condition of these patients by controlling psychological symptoms.

In the studies on health, psychological therapies have been conceptualized more with the word "patient education". Patient education is a necessary section in therapeutic approach for helping the patients with RA because one of the important factors of successful management of this disease is patient education and encouragement of these patients to have proper and correct self-managerial behaviors. Cognitive–behavioral stress management is also one of the mental–social interventions which instruct new cognitive method (such as cognitive reconstruction, coping skills education) and interpersonal skills (such as anger control and assertiveness) (Antoni, 2003).

Cognitive–behavioral stress management has been designed as an intervention for facilitating mental-social adjustment among the physically ill persons. This method is a combination of relaxation techniques and cognitive–behavioral techniques. Based on this intervention method, incidence of depression has been reduced among the women who have been afflicted with breast cancer and its effects continued until 3-month follow-up person. In the study by Mc–Gregor, Antoni, Boyer, Alfer, Blomberg, Carver. (2004), effect of this method on reproduction of lymphocytes has been reported among the patients with breast cancer. Regarding infrastructural mechanisms of effects of this psychological intervention method, McGregor and Antoni (2009) mentioned its effect on the hormone neural system (cortisol) and indices of immune

function, particularly reproduction of lymphocytes and production of cytokines.

The studies which have been conducted on effectiveness of cognitive–behavioral therapeutic method among the patients with chronic physical symptoms are older than those which have been conducted on other psychological therapeutic methods. Effectiveness of this method in reduction of the symptoms and functional disability (Lerman,., 1987), considerable improvement in involvement of joints and reduction of CRP immune index (Sharp, Sensky & Allurd, 2001), fatigue and depression (Evers, Kraaimaat, Geenen & Bijlsmav, 2002), alleviation of pain, fatigue, increase of ability and self-efficacy (Hammon, Bryan & Hardy, 2008, and Holt-Lunstad, Steffen, Sandberg, Jensen, 2011), psychological stress and immune index ESR (Barsky, Alern, Orav, Nestoriuc, Liag, Berman, et al., 2010), and fear of disease progress (Herschbach, Berg, Waadt, Duran, Engst-Hasteiter, Henrich, et al., 2010) have been reported.

Considering the effects which the cognitive–behavioral stress management method leave on the mood and psychological and biological indices of the patients released from breast cancer, the researchers have studied results of cognitive–behavioral stress management program in 5-year and 11-year follow-up to study stability of these results in long term . The result of these two studies indicates that mental-social interventions can have long-term psychological effects on welfare of the patients released from breast cancer at the beginning of treatment and reduce risk factor of mortality rate in this group (Stagl, Antoni, Lechner, Bouchard, Blomberg, Cluck, et al., 2015 ; Stagl, Lechner, Carver, Bouchard, Gudenkaul, Jutagir, et al 2016).

The extensive studies on effectiveness of cognitive–behavioral stress management with patients with HIV showed that the short-term therapeutic behavior has been effective in reduction of mental-social stress and also increase of health. In addition, it also reduces therapeutic costs among the populations of patients (Kirby, Williams, Hocking, Lane & Williams., 2006). This intervention method has been also found to be effective in increase of public health and psychological welfare of the cardiovascular patients (Daneshvari Fard & Mojtanaee, 2016) so that this program led to reduction of Anxiety, anger, and perceived stress in these patients, and these results remained stable for 6 months (Russell, Smith, Krahn, Graskamp, Singh, Kolden, Sigmund, Zhang., 2015). In the study by Sajjadi Nejad, Asgari, Molavi, Adibi. (2015), cognitive–behavioral stress management method was found to be effective in stress and quality of life of the patients with Ulcerative Colitis.

Regarding the chronic fatigue, Hall (2016) and Lattie (2015) attempted to study its effectiveness on immune indices (IL6[1], cortisone arousal levels) and cytokines with this intervention program in the form of telephone sessions. However, considering the obtained results, they did not succeed in identification of effect of this intervention method on these variables from base line to 5 months or 9 months later. Despite unsuccessfulness of these two researchers in holding the effective therapeutic sessions by phone, Schere, Alder, Gaab, Berger, Ihde, Urech. (2016) were able to reduce their anxiety and stress considerably by performing the intervention program among the population of women susceptible to preterm birth.

Today, it was specified that psychological interventions cause positive health outcomes by stimulating the immune system. It is evident that the researches on different interventions beside pharmacotherapy are not only clinically, but also theoretically, important for the fields of psychoneuroimmunology and can add to the

1- Interleukin6

scientific value of this field. Considering this fact and failure to dealing with effectiveness of the psychological treatments in the immune factors among the patients with Rheumatoid arthritis, this study investigated effectiveness of the cognitive–behavioral stress management in reduction of immune, psychological indices, and pain severity of the patients with Rheumatoid arthritis among the local studies to promote physical and mental health level of the patients with Rheumatoid arthritis.

Method

Participants

The statistical population of the present research includes patients referred to Tehran Rheumatology clinic. Among them, 40 patients with Rheumatoid arthritis were selected through purposive sampling method by observing the inclusion criteria and the test and control groups each with 20 subjects. These two groups were peer in terms of inclusion and exclusion criteria.

Inclusion criteria of the subjects

1- Indication of Rheumatoid Arthritis by Physician's criteria based on the clinical examinations and tests, 2- affliction with RA disease at least 6 months, 3- having literacy , 4- being in the age range of 25 to 60 years.

Exclusion criteria

1- The patients with brain organic symptoms, 2- affliction with Fibromyalgia, 3-antidepressent drug consumers, 4- history of anxiety and depression or other mental diseases before affliction with Rheumatoid arthritis,5 - affliction with any uncontrolled disease such as diabetes and migraine, 6- affliction with severe Rheumatoid arthritis.

For ethical consideration, the consent of patients was gained for the participation in the study. Also patients were assured that their information will remain confidential and their name and addresses will not be mentioned elsewhere. Therapy sessions were arranged after the study for the control group members who were on the waiting list.

Procedure

The present research is based on Quasi experimental method in which effectiveness of an independent variable (Cognitive–behavioral stress management) on the dependent variables (immune factors: CRP, ESR and psychological, depression, anxiety, stress, and pain severity) has been studied considering the moderating variables (age, gender, and education). On this basis, pretest, posttest, and control group is used.

Both groups were studied before participation in the intervention sessions with the research instruments including depression, anxiety and stress test (DASS) and blood sample including CRP and ESR factors. The intervention program which has been used in this research is the cognitive–behavioral stress management program. The general structure of this intervention is quoted from the book written by Antoni (2007) and eight 2-hour sessions were held by the educated physiologist in a group in summer and fall 2014 in Dr. Bayat Rheumatology Clinic. The sessions included methods of reduction of anxiety based on progressive relaxation education and abdominal breathing, relaxation education with 16, 8, 8, and 4 muscle group, inactive relaxation, autogenic Training for heat, autogenic Training for heartbeat, breathing, abdomen and forehead along with Mantra meditation, and illustration. The cognitive reconstruction education included cognitive errors, automatic thoughts and negative beliefs and challenging them, training of Cognitive–behavioral coping skills. Data of this research was analyzed through MANCOVA with SPSS 19.

Sessions	Sessions content
First session	Familiarity, creation of motivation, review of sessions structure, creation of a good therapeutic relation along with sympathy and listening
Second session	Familiarity with concept of stress and stress symptoms, role of stress in start , severity and continuity of Rheumatoid arthritis, discussion about roots, internal and external factors of stress, and explanation of relaxation
Third session	Relationship between thoughts and feelings and ways of illogical thoughts recognition and explanation of processing errors and reassessment education and thoughts and challenging of thoughts as strategies of challenging illogical thoughts, muscular relaxation technique, 8 muscle groups and 4 muscle groups
Fourth session	Coping with stress, exercise and class activity relating to the previous discussions, discussion of the stressful positions and education of stress coping skills, breathing, illustration and inactive muscular relaxation
Fifth session	Replacement of logical thoughts with illogical thoughts, heaviness and heat autogenic training
Sixth session	Studying efficient and inefficient stress coping strategies, autogenic training for heartbeat, breathing and abdomen
Seventh session	Anger management, autogenic training along with illustration and self-induction
Eighth session	Review of the discussions of the past sessions, delivery of the discussion content and the recorded voice in the sessions in the form of pamphlets and CD, execution of the second assessment stages
Ninth session	Relationship between thoughts and feelings and ways of recognition irrational thinking and explanation of processing errors and thoughts reassessment training, challenging of thoughts as strategies of challenging irrational thinking, muscular relaxation technique, 8 muscle groups and 4 muscle groups

Measures

Depression, Anxiety, Stress Scale (DASS)

This scale contains 21 questions and is scored based on Likert scale. Antoni. (1998) factor analyzed the scale and their research results indicated the presence of three mental factors of depression, anxiety, and stress. Results of this study showed that 68% of the total variance of the scale was measured by these three factors. Special values of these factors, i.e. depression, anxiety, and stress, in the research were equal to 0.97, 0.92 and 0.95 respectively. Results of calculation of correlation between the factors in the study by Antoni et al. indicated the correlation coefficient of 0.48 between two factors of depression and stress, correlation coefficient of 0.51 between anxiety and stress, and correlation coefficient of 0.28 between anxiety and depression. Validity of the questionnaire in Iran was studied by Samani and Jokar (2007) and retest validity for depression, anxiety, and stress scales were 0.81, 0.76, and 0.77 respectively, and Cronbach's alpha for the depression, anxiety, and stress scales were 0.81, 0.74, and 0.78, respectively. Divergent and convergent validity and construct validity (factor analysis) were also confirmed.

McGill pain inventory

This variable is assessed through McGill pain inventory. McGill pain inventory is the most reliable tool for measurement of chronic pains which has scientific validity and reliability. This questionnaire includes 15 cases related to sensual and emotional components of pain, graded visual criterion of pain with score of 0-10, and one of the 5 criteria of pain severity (without pain to severe pain) and the maximum score was 59 (Keshavarz, Dadgari & Miri, 2008).

Cronbach's alpha coefficient of the inventory is 0.85 and reliability coefficient in all of the fields was above 0.8. Reliability coefficient of the constituent groups keeps significant relationship during test period (Khosravi, Sedigi, Moradi., 2012).

Results

The mean age of the sample group was 1.49±47.76, and mean duration of disease in most of them was 5.441±5.46. It is necessary to note that both groups became peer in terms of age, gender, and education. Considering that ANOVA is one of the parametric tests, the hypothesis of normality of distribution and homogeneity of covariance and equality of the variances were examined.The Results of testing these hypothesis were shown the equality of variances (with Levin test) and normality of test (Kolmogorov-Smirnov)

Mean and standard deviation of the scores of psychological indices, immunity, and pain of patients in two test and control groups in the pretest and posttest stages are given in Table 1.

Table 1: Mean and standard deviation of the scores of psychological indices, immunity, and pain of patients in two test and control groups in the pretest and posttest stages

		N	Post test		pretest	
Groups	**variables**		**SD**	**min**	**SD**	**min**
Exp	stress	20	9/31	16/85	8/92	19/3
Con		22	10/93	22	10	22/636
Exp	Depression	20	8/81	9/2	7/69	10/1
Con		22	10/76	17/04	11/35	15/182
Exp	anxiety	20	8/71	9/25	6/68	10/9
Con		22	10/76	17/04	11/35	15/182
Exp	ESR	20	7/94	15/01	6/09	15/327
Con		22	8/9	16/13	8/02	13
Exp	CRP	20	0/181	0/144	0/324	0/374
Con		22	0/264	0/374	0/261	0/209
Exp	pain	20	9/73	13/4	10/54	17/15
Con		22	13/73	21/909	12/8	20/574

Using MANOVA to determine effectiveness of cognitive–behavioral stress management on psychological indices (stress, depression, and anxiety), results indicate that this intervention method did nit reduce psychological indices ($F_{3,35}$=1/789,P=0/167, η^2 = 0/133) (Table 2). Effectiveness of this method for each of the psychological indices of stress ($F_{1,37}$= 1/735, P= 0/417, η^2=0/018), depression ($F_{1,37}$=4/318, P= 0/046, η^2 =0/104), and anxiety ($F_{1,37}$= 3/273, P= 0/079, η^2 =0/081) showed that only index of depression was affected by membership in the cognitive–behavioral stress management. According to the effect of this method, it is also evident that intervention of cognitive–behavioral stress management has been more effective in reduction of depression than other variables.

Table 2- Results of MANOVA for effect of group membership on psychological indices (stress, depression, and anxiety)

Effect				**$F_{3,35}$**	**P**	**η^2**
	Stress		0/620	7/155	0/001	0/38
Pretest	depression	Λ	0/676	5/582	0/003	0/324
	Anxiety		0/609	7/478	0/001	0/391
group		Λ	0/867	1/789	0/167	0/133

Results of MANOVA to determine effectiveness of cognitive–behavioral stress management on pain of the patients with Rheumatoid arthritis (Table 3) also showed that this intervention method was effective on alleviation of pain ($F_{1,39}$= 4/885, P=0/033, η^2 =0/111). Effect of this intervention method on alleviation of pain is 11%. It means that 11% of the variance of scores in both groups results from effect of group membership.

Table 3- Results of MANOVA for effect of intervention method of cognitive–behavioral stress management on pain severity

Effect	**SS**	**MS**	**$F_{1,39}$**	**P**	**η^2**
pretest	2658/048	2658/048	33/585	0/000	0/463
Group	386/602	386/602	4/885	0/033	0/111
Erroe	3086/57	79/143			

By studying effectiveness of intervention of stress management on the immune indices (ESR and CRP) (Table 4), it was shown that this intervention method had significant effect on the reduction of immune indices ($F_{2,37}$= 8/703, P= 0/001, η^2 =0/32. In

fact, 32% of the difference of means results from the effect of membership.

Table 4- Results of MANOVA for effect of group membership on rate of immune indices (ESR and CRP)

Effect				$F_{2,37}$	P	η^2
Pretest	ESR	Λ	0/564	14/31	0/001	0/439
	CRP		0/841	3/503	0/04	0/159
group		Λ	0/68	8/703	0/001	0/32

Effectiveness of this method regarding each of the immune indices of ESR ($F_{1,38}$= 1/569, P= 0/218, η^2 =0/04) and rate of CRP ($F_{1,38}$= 17/593, P= 0/001, η^2 =0/316) showed that immune indices of CRP was affected by membership in the intervention method of cognitive–behavioral stress management. Based on the effect of this method, it is evident that intervention of cognitive–behavioral stress management has been more effective in reduction of CRP.

Discussion and conclusion

In this study, the effect of intervention of cognitive–behavioral stress management on psychological indices (stress, depression, and anxiety), immunity (ESR and CRP), and pain severity of the patients with Rheumatoid arthritis was studied. By executing this mental–social intervention, experience of chronic Rheumatoid arthritis was used as an opportunity for training strategies based on stress management.

Besides to its effect on psychological index of depression, CRP immunity index and pain severity of these patients were reduced due to the effect of intervention of stress management.

This finding has been mentioned to support the experienced advantages of this method regarding physical manifestations concurrent with psychological effects. In this regard, it is necessary to note that intervention of cognitive–behavioral stress management includes principles and techniques which aim to reduce stress and negative emotions by creating general comforting response. Different studies reported effects of this relaxation training on automatic changes or in the stress stimulating condition on reduction of cardiovascular reaction and galvanic stimulations (Lehrer, 1972, 1978; Paul, Trimble, 1970; Pawlow, Jones, 2002, 2005; Conral & Roth, 2007).

Based on the results of these studies, it seems that cognitive–behavioral stress management among the patients with Rheumatoid arthritis in short term is not so effective in reducing stress of the patients. This finding is in line with the results of the study by De Brouwer et al. (2011) and Van Middendorp (2008). De Brouwer believes that stress management education not only does not improve psychological function among these patients, but also can add mental–physiological responses to stress. In fact, emergence of this condition may be a reflection of the repetitive talks about stressful activities and also an increase in awareness of patients with their inability. This explains the fact that since the anxious and depressed clinical patients we excluded from the study like other studies and of the fact that these psychological indices has been reported to be anxiety and stress at medium or mild level, it is expected to achieve this result (Dixon, Keefe, Scipio, Perri & Abernethy, 2007; Barlow, Turner & Writght, 2000; Riemsma, Kirwan, Taal & Rasker, 2002; Astin, Beckner, Soeken, Hochberg & Berman, 2002).

One of the problems which is encountered in this experimental study and inhibits generalization of findings to real condition is consideration of the strict inclusion and exclusion criteria. Of course, lack of progress in two indices of stress and anxiety in the form of intervention method of that cognitive–behavioral stress management should not be generalized to other diseases or other types of intervention.

The other point is that the people vary in coping with disease and this is due to their characters, their experience of disease, economy, culture and social factors. In fact, some people tend to apply their personal style for adjustment to the stress (Vailant,

1979).

In this regard, duration of disease is very important because if duration is long, the patients during this term learn coping methods. In fact, the chronic patients may have stronger interventions. Considering that duration of the disease among the patients participating in this study has been approximately 5 years, this hypothesis can hold true.

Since depression among the patients with RA is 2-3 times as prevalent as the general population, these symptoms can be an important goal of intervention among this population. In fact, one of the main causes of depression among these patients is reduction of physical activity. Among them, many psychological interventions showed that improvement of motor activities improved pain intensity and inability of the patients (Knittle, Maes & De Gucht., 2010). On the other hand, determination of the behavioral goals and achieving them strengthen patients and reduce anxiety and negative thoughts about life among them. In other studies, the perceived control and personal efficacy have reverse relationship with anxiety and depression (Fortubne, Barrowclough & Lobban, 2004; Allan, Johnston, Johnston & Mant, 2007; Paschalides, Wearden, Dunkerley, Bundy & Davies, 2004).

In line with the studies which reported effectiveness of different forms of stress management, cognitive–behavioral stress management among the patients with RA in general activity or biological indices (Leibing, Pfingsten, Bartmann, Rueger & Schuessler, 1999; Smyth, Stone, Hurewitz & Kaell, 1999), painful joints (Shearn & Fireman, 1985), changes in cortisol and cytokine, CRP (Sharp et al., 2001), ESR (leibing et al., 1999), results of the present study also showed effect of cognitive–behavioral stress management on CRP inflammatory index.

This finding has been mentioned to support the experienced advantages of this method regarding physical manifestations concurrent with psychological effects, and also is the response to this question that if such positive effects can be included immune reactions(Antoni et al., 2001) Analysis of this path can be explained as the advantages which this intervention method had. change of the attitude toward self,particularity stronger self-perception and better ability of managing their stress and problems directly resulting from cognitive reconstruction and coping skills education (Lutgendorf , Antoni, Ironson., 1998).

Also creation of deeper feeling of goal in life and more concentration on important goals and priorities, which have close relationship with emotional expression and cognitive processing, are facilitated by the group experience (Horowitz., 1986, Janoff-Bulman., 1992) .

These matters are in contrast with depression symptoms, including hopelessness, aimless, fear of future, poor self perception, guilt feeling and anhedonia

On the other hand, one of the main aspects of this educational plan is to strengthen social support as important and essential aspect for health and is related to positive changes in neural–hormone, cardiac system, and immune system (House, 1982; Uchino, Cacioppo & Kiecolt-Glaser, 1996).

This subject can explain changes which have occurred in immune index of CRP in this study. Effect of the intervention of cognitive–behavioral stress management on change of CRP can be related to changes resulting from changes of moods. On the other hand, based on the results regarding the relationship between immunological factors and moods, Reduction in depression mood and CRP immune index can be also confirmed. Results of the present study are in line with results of the study by Antoni and Lerman (2001), Mc Gregor and Antoni (2009), and Jokar (2009).

For explaining the non significant relations

between changes in CRP index and psychological indices of anxiety and stress can be considered to the use of self-reporting tools and observe exaggeration which most of the patients have about their mental and physical moods. while Reduction of depression of patients, improvement of general condition and alleviation of pain intensity in patients naturally predict changes in the immune index.

Since feeling of pain in these patients is related to other mental and physical variables, its reduction can be predicted by reducing depression symptoms as predictor of pain severity of the patients with RA. This finding is in line with results of the study by Connelly, Keefe, Affleck, Lumley, Anderson, Waters., 2007, Parlar, Fadiloglu, Argon, Tokem and Keser, 2013.

About the limitations of this study, most members participating in two study groups were females, this ratio is justifiable because the women are afflicted with Rheumatoid arthritis three times as much as the men are afflicted. However, it is recommended that an equal ratio be used to consider this variable on enjoyment and effectiveness of this intervention method in future studies.

Since assessment stages have been done in two pretest and posttest sections and no study has been conducted on the effectiveness of this intervention method in the long term, it is recommended that effect of this method be studied in the long term by removing this limitation.

Despite the existing limitations, it seems that intervention method of cognitive–behavioral stress management can be used as a complementary method alongside with the pharmaceutical method to control and improve mental and physical variables due to its advantages.

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