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Mindfulness-based Stress Reduction (MBSR) and Its Effects on Psychoimmunological Factors of Chemically Pulmonary Injured Veterans

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ABSTRACT

Mindfulness-based Stress Reduction (MBSR) is a treatment program for relieving stress and coping with chronic illnesses. In recent three decades, studies have shown that MBSR has a positive effect on physical and psychological dimensions of chronic illnesses. Chemically pulmonary injured veterans have chronic pulmonary and psychological problems due to mustard gas exposure and complications of Iran-Iraq war. These stresses have negative effects on their general health and immune system. To the best of our knowledge, this is the first study conducted on psychoneuroimmunology and MBSR in these patients.

Forty male pulmonary injured veterans were randomly divided in two groups with 20 participants (MBSR and wait-list control). Then MBSR group received 8 weekly sessions of intervention. We tested mental health based on general health questionnaire (GHQ)-28 questionnaire, health-related quality of life (based on St. George respiratory questionnaire (SGRQ)) and immunity in MBSR groups; before and after intervention "mixed factorial analyses of variance" test was used for analyzing data fpr each dependent variable and appropriate t-tests were done in The necessary condition.

Results showed that mental health and health- related quality of life, in MBSR group compared to wait-list control improved [F (1,38)=26.46, p<0.001; F (1,38)=49.52, p<0.001 respectively] significantly. Moreover, a significant increase was reported in the lymphocyte proliferation with phytohemagglutinin (PHA) [F (1,38)=16.24, p<0.001], and peripheral blood IL-17 [F (1,38)=56.71, p<0.001] However, lymphocyte (CD4+, CD8+, and NK-cell) percentages were not affected significantly [F (1,38)=2.21, p=0.14] ,[F (1,38)=0.90, p=0.78] and [F (1,38)=1.79, p=0.18], respectively.

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Mindfulness- based Stress Reduction (MBSR) and Psychoimmunological Factors

This study suggests that MBSR may be a new treatment approach for improving immunity and overall health in chemically pulmonary injured veterans.

Keywords: CD4+; CD8+; IL-17; Lymphocyte proliferation; Mindfulness; Mental health; NK-cell; Quality of life; Veterans

INTRODUCTION

Therapeutic methods of complementary and alternative medicine like mindfulness-based stress reduction (MBSR) have growing popularity and are used for treatment and adjustment to many chronic illnesses.[1,2] MBSR as a self-regulating method needs intentional, moment to moment, non-judgmental attention to here and now, to internal and external experiences, to bodily sensation, thoughts, consciousness, and to environment, while doing some practice such as walking. This is an attention and openness, only to present time because attention to past and future time may create psychological distress like depression and anxiety[3-5]

MBSR is defined as a standardized and manualized 8-week intervention developed by Kabat-Zinn[4], which has been used widely in medical and behavioral researches. The sessions include breathing relaxation, body scanning, object meditation, mindful eating walking meditation, mindful stretching, worry surfing, and simply watching.

Previous studies showed that MBSR has therapeutic effects on psychological distress, negative mood, depression and anxiety in many patients and normal populations including women with early-stage breast cancer[6,7] , somatization disorder and functional somatic syndromes[8], Biologic and Emotional disorders Among Older Adults,[9] heterogeneous anxiety disorders,[10] mental illness,[11] comorbid anxiety and depression,[12] decreased emotional wellbeing and quality of life in percutaneous coronary intervention patients,[13] generalized anxiety disorder,[14] HIV/AIDS patients,[15] stress-related psychological distress in healthcare professionals,[16] glycemic control in type 2 diabetes mellitus,[17] mood and symptoms of stress in cancer outpatients,[18] nurse stress and burnout,[19] symptoms of stress and levels of cortisol and melatonin in breast and prostate cancer outpatients[20] and psychological distress in medical students.[21]

Many studies showed that MBSR has positive effect on quality of life of different patients.[6,7,13,17,20,22,23]

Regarding the effect of MBSR on immunological factors, studies showed positive results for example: a study has shown that increased production of IL-4 and decreased levels of IFN-γ and IL-10 in breast and prostate cancer outpatients.[23] In breast cancer patients who received MBSR after chemotherapy, increased peripheral blood mononuclear cell, NK cell activity (NKCA), IFN gamma, IL-4, IL-6, and IL-10 production, and plasma cortisol levels were observed over time. [24] Moreover, increased lymphocyte proliferation by phytohaemagglutinin (PHA), Th1/Th2 ratio, and CD4+ count have been reported after MBSR in patients with breast cancer[25]. In another study a protective role against CD4+ loss in HIV-1-infected adults 25 have been observed.[26]

We chose IL-17 from all other types of interleukins because numerous immune regulatory functions have been reported for the IL-17 family of cytokines, presumably due to their induction of many immune signaling molecules. The most notable role of IL-17 is its involvement in inducing and mediating pro-inflammatory responses. IL-17 is commonly associated with allergic responses. IL-17 induces the production of many other cytokines (such as IL-6, G-CSF, GM-CSF, IL-1β, TGF-β, TNF-α), chemokines (including IL-8, growth-regulated protein alpha (GRO-α), and monocyte chemoattractant protein-1(MCP 1)), and prostaglandins (e.g., PGE2) from many cell types (fibroblasts, endothelial cells, epithelial cells, keratinocytes, and macrophages). The release of these cytokines causes many reactions including airway remodeling, a characteristic response induced by IL-17. The increased expression of chemokines attracts other cells including neutrophils but not eosinophil. IL-17 function is also essential for a subset of CD4+ T-Cells called T helper 17 (Th17) cells. Considering the variety of its functions, the IL-17 family has been linked to many immune/autoimmune-related diseases including rheumatoid arthritis, asthma, systemic lupus erythematosus, allograft rejection, anti-tumor immunity, and recently psoriasis and multiple sclerosis.[26-29]

After mustard gas exposure in the Iraq-Iran war three decades ago, Iranian chemically pulmonary injured veterans have faced many persistent stressors like chronic pulmonary problems, and other stresses (because of war complications and their illness in life. These

stresses have negative effect on their general health and immune system. On the other hand most of the treatments that have been used for them are chemical drugs and palliative therapies. Thus development of new non-drug interventions that can improve health, immunity and quality of life is essential in their rehabilitation program.

To the best of our knowledge no other studies have been done to evaluate MBSR and its effects on these patients; therefore, we designed this study with the assumption that this intervention will improve psychoimmunological condition and quality of life in chemically pulmonary injured veterans.

MATERIALS AND METHODS

Participants

Participants (n=40) were male veterans with pulmonary injury due to mustard gas exposure in Iran-Iraq war (age 42-59; mean=49.40).

This study was conducted under the supervision of the ethics committee of Baqiyatallah University of Medical Sciences. After the briefing session all subjects signed the informed consent forms.

Inclusion Criteria

All of the patients were Caucasian and inhabitant in the city of Tehran. They had mild to moderate pulmonary problems (based on Gold criteria)[28] with negative history of acute psychotic disorder or psychosis, psychiatric drug consumption, and any chronic medical problem except sequels of chemical injuries. All cases had record files in a respiratory diseases clinic and were under regular observation. . In the process of assigning subjects to groups, we controlled the inclusion criteria and accordingly balanced two groups

Procedure

Participants were asked to complete study measuring tools; general health questionnaire (GHQ), and St. George respiratory questionnaire (SGRQ) [30]. Then, they were referred to Pasture Institute of Iran, for immunological tests. After this first evaluation, they were randomly divided in two groups; MBSR group (n=20) and wait-list (WL) control group (n=20) using computerized number generator. MBSR group received eight sessions of MBSR. MBSR was administered by a clinician specialist and consisted of eight weekly 120-minute group sessions, and one session of daily home practice. After the 8-week-period, all participants completed the same questionnaires as of the first evaluation. During this 8-week period, WL group were asked not to participate in any new intervention or treatment and received MBSR program after second evaluation.

Measures and Data Analytic Approach

GHQ-28

The GHQ questionnaire as a screening tool for detecting psychiatric problems was first developed in 1978 by Goldberg. It has four subscales including; "somatic symptoms" (items1-7), "anxiety/ insomnia"(items8-14)," social dysfunction" (items15-21) and "depression" (items 22-28).[30]

The St. George's Respiratory Questionnaire

SGRQ was developed by Jones et al. as a self-administered and standardized pulmonary disease-specific questionnaire. It has 50 items in 76 levels and three subscales: "Symptoms" including frequency and severity of several respiratory symptoms (8 items), "Activity" includes activities that cause or decrease breathlessness (16 items), and "Impacts" including psychological problems and social functioning resulted from pulmonary disease (26 items).[31]

Immunology Tests

Lymphocyte Proliferation Test (LTT)

LTT is the most widespread functional in vitro assessment of the immune system. It measures lymphocyte proliferation in response to stimuli. The basic assumption in this test is: "the greater proliferation, the more effective immune response".[32]

Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized blood by density gradient centrifugation over Histopaque-1077 (Sigma Aldrich, St. Louis, MO, USA). PBMCs (4×105) were distributed in duplicate in 96-well microtitre plates (SPL, South Korea) in a final volume of 200 u, with phytohaemagglutinin (PHA, 15ug/mL, Gibco, USA), ConA (5ug/mL, Sigma-Gibco, USA) or medium as control. Briefly 4×105 viable cells were cultured in Roswell Park Memorial Institute medium (RPMI) with 10 mM (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid)(HEPES), supplemented with 2 mm L-glutamine, 10% heat-inactivated fetal bovine serum (FBS), 100 U/mL penicillin, and 100 mg/mL streptomycin.

Cultures were incubated for 4 days and processed for incorporation of [3H]-thymidine.

ELISA (Cytokine Assays)

The supernatant of cells in 24 well plates (cultured as above mentioned) 72 h after stimulation were collected, stored at -70°C, then concentration of IL-17 was measured by sandwich ELISA technique using commercial kits (eBioscience, San Diego, CA, USA) according to manufacturer's procedure. Samples were measured in duplicate.

Flow Cytometric Analysis (FACS)

After blood vortex and adding 20 µL of CD4+, CD8+ and NK cell-specific monoclonal antibodies conjugated with fluorescent dye iQ SYBR® Green Supermix Poland) to 100 µL whole blood, samples were incubated for 20 min at room temperature in the dark. After incubation, 2 mL red blood cell lysis solution (Miltenyi Biotec Inc, Auburn, CA, USA) was added and then centrifuged for 7 min at 400 g and 4°C, to separate the red cell lysate. After that, white blood cells were washed with phosphate-buffered saline (PBS) solution in the centrifugation as before. 1 mL PBS was added to precipitation of white blood cells preparing it to be read by flow cytometers.

Data Analysis

The study had a mixed factorial 2×2 design, including within subject (two times evaluation) and between subject (with and without intervention) factors. We used "mixed factorial analyses of variance" test for analyzing data in each dependent variables. Then, if we found significant interaction effect, we used "paired-samples T test" for comparing before and after intervention data of each group (Table 1), and "independent-samples T test" for comparing after intervention data of two groups (Table 3). These analyses were done for each dependent variable separately.

RESULTS

Preliminary Analyses

The MBSR and WL groups did not significantly differ in any dependent variables at baseline (before the intervention) as shown in Table 2, which indicated successful randomization.

MBSR Training and GHQ

The MBSR reduced GHQ total score compared to WL condition. A mixed effect linear model revealed a significant treatment condition×time interaction in GHQ total score (F (1, 38) =26.46, p<0.001) (Table 2). Specifically, MBSR participants showed significant decreases in GHQ score comparing before and after intervention (t=11.10, p<0.001). While WL group's showed significant increases comparing before and after intervention (t=0.57, p<0.001) (Table 3). As an additional test to evaluate MBSR effects on GHQ total score, we conducted follow-up independent sample t-test in our subsamples: MBSR participants had lower GHQ total score after intervention compared to WL participants (t=-3.70, p<0.001.001) (see Table 4), after controlling for baseline GHQ total score.

As mentioned in Table 3 and 4 the MBSR reduced "somatic symptoms", "anxiety/insomnia", "social dysfunction ", "depression" subscales score subscale score of GHQ comparing to WL group. p<0.001) (Table 3).

MBSR Training and Health-related Quality of Life

The MBSR reduces SGRQ total score comparing to WL condition, a mixed effect linear model revealed a significant treatment condition× time interaction in SGRQ total score (F (1, 38) =49.52, p<0.001) (Table 2). Specifically, MBSR participants showed significant decreases in SGRQ total score from before the intervention to after intervention (t=10.67, p<0.001) compared to no significant change from before the intervention to after intervention in WL group (t=-1.41, p<0.001.17) (Table 3). AS an additional test of MBSR effects on SGRQ total score, we conducted follow-up independent- sample t-test in our subsample: MBSR participants showed lower SGRQ total score at after intervention comparing to WL participants (t=-2.81, p<0.001.007) (see Table 4), after controlling for baseline SGRQ total score.

As mentioned in table 3 and 4 the MBSR reduced "Symptoms", "activity" and "impact" subscales score of SGRQ comparing to WL condition.

MBSR Training and LTT with ConA

The MBSR increases LTT (SI)-ConA comparing to WL condition, a mixed effect linear model revealed a significant treatment condition × time interaction in LTT (SI)-ConA (F (1,38)=8.90, p<0.001.005) (Table 2). Specifically, MBSR participants did not show

significant increases LTT (SI) - ConA from before the intervention to after intervention (t=-0.95, p<0.001.35) compared to significant decreases from before the intervention to after intervention in WL group (t= 6.96, p<0.001) (see table 3). AS an additional test of MBSR effects on LTT (SI)-ConA, we conducted follow-up independent- sample t-test in our subsample: MBSR participants showed higher LTT (SI)- ConA at after intervention compared to WL participants (t=5.40, p<0.001) (Table 4), after controlling for baseline LTT (SI)-ConA.

Table 1. Effects of mindfulness based stress reduction on all dependent variables of general health questionnaire and St. George's respiratory questionnaire

	Group	Pre mean	SE	Post mean	SE	F- value	*p*-value
GHQ-Total	MBSR	50.92	2.37	36.22	2.43	26.46	≤0.001
	WL	52.21	3.77	50.93	3.13		
GHQ-Somatic Symptom	MBSR	13.22	0.60	9.44	0.47	17.91	0.001
	WL	9.44	0.80	13.83	0.69		
GHQ-Anxiety/Insomnia	MBSR	16	0.56	10.33	0.68	31.08	≤0.001
	WL	15	1.04	14.70	0.80		
GHQ-Social Dysfunction	MBSR	12.22	0.68	9.11	0.70	13.16	0.001
	WL	13.12	1.08	12.84	0.90		
GHQ-Depression	MBSR	9.44	1.01	5.77	0.81	18.89	≤0.001
	WL	9.08	1.29	9.46	1.28		
SGRQ-Total	MBSR	80.81	2.10	67.58	2	49.52	≤0.001
	WL	77.49	4.73	80.15	3.94		
SGRQ-Symptom	MBSR	89.50	0.71	77.86	1.64	21.31	≤0.001
	WL	83.05	3.65	88.76	2.67		
SGRQ- Activity	MBSR	74.47	3.60	68.29	2.21	15.66	≤0.001
	WL	76.22	5.42	82.36	4.20		
SGRQ- Impact	MBSR	75.59	3.40	54.32	3.05	38.11	≤0.001
	WL	68.40	6.29	70.27	5.92		
LTT(SI)- ConA	MBSR	20.5	2.04	23.25	2.75	8.90	0.005
	WL	16.55	1.80	7.30	0.91		
LTT(SI)- PHA	MBSR	26.05	2.16	34	2.99	16.24	≤0.001
	WL	22.15	3.18	12	0.81		
IL-17	MBSR	178.12	18.90	382.31	36.68	56.71	≤0.001
	WL	140.58	31.05	158.18	26.16		
CD4+ percentage	MBSR	48	1.43	45.05	1.53	2.21	0.14
	WL	51.06	1.75	51.07	1.87		
CD8+ percentage	MBSR	36.21	1.73	36.47	0.95	0.90	0.78
	WL	37.16	0.96	38.13	1.04		
NK-cell percentage	MBSR	6.28	0.58	5.10	0.96	1.79	0.18
	WL	6.44	0.86	7.36	1.10		
	WL						

Note: Means and standard errors (SE) at pre and post intervention in the MBSR and WL groups for all variables. F and corresponding *p*-values refer to the treatment condition × time interaction

MBSR: mindfulness based stress reduction; WL: wait-list; GHQ: general health questionnaire; SGRO: St. George's respiratory questionnaire; LTT: lymphocyte transformation test; CONA: concanavalin A; PHA: phytohaemagglutinin

Table 2. Scores of general health questionnaire, St. George's respiratory questionnaire and laboratory characteristics of chemically pulmonary injured veterans and control group before intervention (mindfulness based stress reduction)

Variable	MBSR Group	WL Group	Statistical Difference
Age	50,20 (5.25)	48.60 (4.63)	t=1.02 , *p*=0.31
GHQ-TOTAL	50.22 (10.63)	52.21 (16.86)	t=-0.29 , *p*=0.77
SGRQ – TOTAL	75.59 (9.39)	68.40 (29.18)	t=.64 , *p*=1.52
LTT(SI)- CONA	20.15 (9.15)	16.55 (8.06)	t=1.31 , *p*=1.19
LTT(SI)- PHA	26.05 (9.66)	22.15 (14.22)	t=1.01 , *p*=1.31
IL-17	178.12 (84.56)	140.58 (138.89)	t=1.03 , *p*<0.001.3
CD4+ percentage	48 (6.40)	51.06 (7.85)	t=-1.34 , *p*<0.001.18
CD8+ percentage	36.21 (7.74)	37.16 (4.33)	t=-0.48 , *p*<0.001.63
NK-cell percentage	6.28 (2.63)	6.44 (3.88)	t=-0.15 , *p*<0.001.88

Note: Standard deviation values are presented in parentheses

MBSR: mindfulness based stress reduction; WL: wait-list; GHQ: general health questionnaire; SGRO: St. George's respiratory questionnaire; LTT: lymphocyte transformation test; CONA: concanavalin A; PHA: phytohaemagglutinin

Table 3. Paired samples T test in mindfulness based stress reduction and waiting list groups

Variable	Group	Mean Diff (Before and After of each group)	T
GHQ-Total	MBSR	14.69	11.10 , *p*≤0.001
	WL	1.28	0.57 , *p*<0.001
GHQ-Somatic	MBSR	3.77	9.38 , *p*≤0.001
Symptom	WL	0.96	1.82 , *p*<0.001
GHQ-	MBSR	5.66	12.35 , *p*≤0.001
Anxiety/Insomnia	WL	0.69	0.91 , *p*<0.001
GHQ-Social	MBSR	3.11	6.36 , *p*≤0.001
Dysfunction	WL	0.28	0.46 , *p*<0.001
GHQ-Depression	MBSR	3.66	5.83 , *p*≤0.001
	WL	-0.38	-0.55 , *p*<0.001
SGRQ-Total	MBSR	13.22	10.67 , *p*≤0.001
	WL	-2.66	-1.41 , *p*<0.001
SGRQ-Symptom	MBSR	11.65	6.16 , *p*≤0.001
	WL	-5.68	-1.75 , *p*<0.001
SGRQ- Activity	MBSR	6.17	2.68 , *p*<0.001
	WL	-6.13	-2.93 , *p*<0.001
SGRQ- Impact	MBSR	1.19	-12.59 , *p*≤0.001
	WL	-1.86	-0.78 , *p*<0.001
LTT(SI)- ConA	MBSR	-3.10	-0.95 , *p*<0.001
	WL	9	6.96 , *p*≤0.001
LTT(SI)- PHA	MBSR	-7.95	-2.19 , *p*<0.001
	WL	10.15	3.82 , *p*<0.001
IL-17	MBSR	-204.10	-9.09 , *p*≤0.001
	WL	-176	-1.67 , *p*<0.001

Diff : differentiation; MBSR: mindfulness based stress reduction; WL: wait-list; GHQ: general health questionnaire; SGRO: St. George's respiratory Questionnaire; LTT: lymphocyte transformation test; CONA: concanavalin A; PHA: phytohaemagglutinin

Table 4. Independent sample T-test between mindfulness based stress reduction and waiting list groups

Variable	Group	Mean Diff	T
GHQ-Total	MBSR WL	-14.71	-3.70, $p<0.001$
GHQ-Somatic Symptom	MBSR WL	-4.39	-5.21 , $p\leq0.001$
GHQ-Anxiety/Insomnia	MBSR WL	-4.37	-4.15 , $p\leq0.001$
GHQ-Social Dysfunction	MBSR WL	-3.73	-3.24, $p<0.001$
GHQ-Depression	MBSR WL	-3.69	-2.42 , $p<0.001$
SGRQ-Total	MBSR WL	-12.56	-2.81 , $p<0.001$
SGRQ-Symptom	MBSR WL	-10.90	-3.47 , $p<0.001$
SGRQ- Activity	MBSR WL	-14.06	-2.96 , $p<0.001$
SGRQ- Impact	MBSR WL	-15.94	-2.39 , $p<0.001$
LTT(SI)- ConA	MBSR WL	15.70	5.40 , $p\leq0.001$
LTT(SI)- PHA	MBSR WL	22	7.08 , $p\leq0.001$
IL-17	MBSR WL	224.13	4.78 , $p\leq0.001$

MBSR: mindfulness based stress reduction; WL: wait-list; GHQ: general health questionnaire; SGRO: St. George's respiratory questionnaire; LTT: lymphocyte transformation test; CONA: concanavalin A; PHA: phytohaemagglutinin

MBSR Training and LTT with PHA

The MBSR increases LTT (SI)- PHA comparing to WL condition, a mixed effect linear model revealed a significant treatment condition× time interaction in LTT (SI)- PHA (F (1,38)=56.71, $p<0.001$) (Table 2). Specifically, MBSR participants showed significant increases LTT (SI) - PHA from before the intervention to after intervention (t=-2.19, $p<0.001.04$) compared to significant decreases from before the intervention to after intervention in WL group (t= 3.82, $p<0.001.001$) (Table 3). AS an additional test of MBSR effects on LTT (SI) - PHA, we conducted follow-up independent-sample t-test in our subsample: MBSR participants showed higher LTT (SI) - PHA at after intervention compared to WL participants (t=7.08, $p<0.001$) (Table 4), after controlling for baseline LTT (SI)- PHA

MBSR Training and IL-17 ELISA

The MBSR increases IL-17 compare to WL condition, a mixed effect linear model revealed a significant treatment condition× time interaction in IL-17 (F (1,37)=56.71, $p<0.001$) (Table 2). Specifically, MBSR participants showed significant increases IL-17 from before the intervention to after intervention (t=-9.09, $p<0.001$) compared to no significant changes from before the intervention to after intervention in WL group (t= -1.67, $p<0.001$) (Table 3). AS an additional test of MBSR effects on IL-17, we conducted follow-up independent-samples T test in our subsample: MBSR participants showed higher IL-17 at after intervention compared to WL participants (t=4.78, $p<0.001$) (Table 4), after controlling for baseline IL-17.

MBSR Training and Lymphocyte Percentage

Three mixed effect linear models revealed no significant treatment condition × time interactions in "CD4+ percentage" (F (1,38)=2.21, $p<0.001$), in "CD8+ percentage" (F (1,38)=0.90, $p<0.001$) and in "NK-cell percentage" (F (1,38)=1.79, $p<0.001$).

DISCUSSION

Wars during the past two decades have caused many psychological problems. Therefore, the number of studies carried out on stress management in veterans have increased, one of the methods used in such studies is MBSR.[33-36] Previous studies on chronic medical diseases and psychological disorders, and even some normal populations, suggest a role for MBSR in reducing psychological distress, depression, anxiety, and other psychological factors, along with improving quality of life and immunological factors.[6-10,12-18,20-22] However, This is the first study in chemically pulmonary injured veteran's population that shows MBSR can affect immunological factors.

Findings of the present study show that MBSR can improve immunological factors, mental health and health-related quality of life in chemically pulmonary injured veterans.

The findings of the this study suggesting improvements of mental health, and reducing depression and anxiety are paralleled with results of many other studies; reduction in psychological distress, negative mood, depression and anxiety have been shown in patients with cancers,[5,9,10,17,18,20,23,37] in patients with psychiatric disorders,[7,9,12,14,38] in healthy people with high psychological distress like medical students, nurses, healthcare professionals and older adults[9,16,17,21,42]in percutaneous coronary intervention (PCI) patients,[13] in type 2 diabetes mellitus patients,[17] and in Iranian HIV/AIDS patients.[15]

Results of our study in improving health-related quality of life; reducing frequency and severity of pulmonary symptoms like cough and wheezing, improving activities that cause or limited by breathlessness, reducing impacts of disease on patient's life (means psychological problems and social functioning resulted from pulmonary disease), are paralleled to many studies that have shown MBSR has positive effects on quality of life in woman with breast cancer,[6] in patients with prostate and breast cancer,[20,23,38-39] in patients with somatization disorder[8], in reducing stress among nursing personnel[19,20] Measures of depression and quality of life in veterans,[34,35] in percutaneous coronary intervention (PCI) patients and in type 2 diabetes mellitus patients.[13,17]

The finding of our study shows that MBSR can increase lymphocyte proliferation (especially with PHA mitogen) and thereby improves effectiveness of immune response.[29] Furthermore, MBSR can increase IL-17 in peripheral blood of our patients.

IL-17 as a pro-inflammatory cytokine produced by activated memory T cells; has a key role in host's defense against microbial infections[35] and in the initiation and maintenance of inflammatory responses.[36] The T cells that produce IL-17, have important role in controlling inflammatory and immunity reactions.[37] In our study, MBSR has not any effect on CD4+, CD8+ and NK-cell percentages. Immunological changes caused by MBSR in this study, are compatible with findings of other studies, although these studies did not evaluated the quite similar immunological factors. In a study on patients with prostate and breast cancers, MBSR increased production of IL-4 and decreased IFN-γ and IL-10.[23] In women newly diagnosed with early stage breast cancer, Witek-Janusek et al. showed that before MBSR intervention, a reduction of PBMCs, NK-cell activity, and IFN-γ; and increased production of IL-4, IL-6, IL-10, and plasma cortisol level were observed in two groups (MBSR and control), but after MBSR intervention, NK-cell activity and cytokine production were stable in MBSR group, although in control group, reduction of NK-cell activity and IFN-γ production, and increased production of IL-4, IL-6, IL-10 continued. Lengacher et al. [24] showed that in patients with breast cancer, lymphocyte proliferation by PHA, Th1/Th2 ratio and CD4+ count increased with MBSR. In individuals infected with HIV, Robinson et al,[38] reported that in MBSR group, NK-cell activity and count increased. Creswell et al.[41] suggested that MBSR can have a protective role against CD4+ loss in HIV-1 infected adults.

Although limited number of cases is a major limitation of this project, this study on the psychoneuroimmunology of chemically pulmonary injured veterans makes two new contributions to the literature. First, this work provides an initial indication that MBSR can improve individual's immunity and health and Second, MBSR also can improve immunological and psychological functioning, respiratory symptoms, and overall quality of life in these patients.

The results of this study could lead to a change in the approach to treatment of chemically pulmonary injured veterans, who are almost stressful and under influence of chronic pulmonary disease and war time

memories.

MBSR as a safe and non-chemical intervention for these patients can increase their quality of life by decreasing stress and affecting on dependent immunological factors.

Future studies are necessary with larger samples, and control group, examining other immunological factors and controlling variables that may affect the results.

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