A Fresh Look at the Potential Mechanisms of Progressive Muscle Relaxation Therapy on Depression in Female Patients With Multiple Sclerosis

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Background: According to the World Health Organization (WHO) report released in 2000, about 121 million people worldwide suffer from depression. The major depressive disorder (MDD) among multiple sclerosis (MS) patients is one of the most common mood disorders experienced during life. MS patients who simultaneously suffer from depression have reported more severe symptoms of disease and slower adaptation to new conditions, which ultimately increase the cost of treatment.
Objectives: The aim of this study was to assess the effectiveness of progressive muscle relaxation therapy (PMRT) as an adjunctive therapy for reducing level of depression for MS patients.
Materials and Methods: This research had the randomized controlled trial design with pre and posttest. Thirty female patients based on criteria of MS and MDD disease, were selected from the MS Society of Shiraz, Iran. Beck Depression Inventory (BDI-II) was administered at pre and posttest. The participants were randomly allocated to two groups (experimental and control). Twelve sessions of PMRT using Bernstein and Borkovec's method were held for the experimental group. Levin's test, covariance and ANOVA with repeated measures were used for data analysis.
Results: Experimental and control groups were compared before and after treatment. Analysis of covariance showed that seven levels of depression decreased in the experimental group and analysis of repeated measure showed that 49% of the changes were related to PMRT.
Conclusion: According to the results, PMRT is effective in reducing depression. This therapy enables patients to reach relaxation quickly, and thus can cope with depression reactions effectively.

Keywords: Depression; Multiple Sclerosis; Muscle Relaxation; Therapy

1. Background

Multiple sclerosis (MS) is a disease with a variable course. This disease usually occurs with reversible periods of neurological disability during the third and fourth decades of life and finally, in the sixth or seventh decades of life, this disease becomes an irreversible neurological disorder and permanent disability (1). MS disease is demarcated with inflammation and destruction of white matter of the brain and spinal cord and its replacement with gliotic tissue (2). The etiology of disease this unknown, however, strong evidence for irreversible neurological disability in MS patients indicates that MS disease is an autoimmune disease against central nervous system myelin or neuron degeneration (3).

MS disease has been reported 1.8 times more in females than males and has a profound effect on the personal lives of individuals (4). One million people in the world suffer from MS that is comorbid with psychiatric disorders (5). Cognitive impairment is common in this disease (6). Prevalence of cognitive impairment is about 30.5%, and affects attention, concentration, performance, processing speed and visual perception. Non-somatic symptoms of depression, can predict cognitive performance but it is not clear how depression affects cognitive impairment (7).

On the other hand somatic and non-somatic symptoms of depression predict exacerbation of MS disease (8). Therefore, interaction between medical and psychological variables in MS disease is complex. MS disease usually indicates disparate disease periods (4). The cause and cure are unknown; appearance, removal and even relapsing of symptoms occurs without any warning signs (9) and the onset of the disease may be acute or gradual (10).

MS disease may prevent some patients from activities such as, employment, relationships (social, familial and sexual), goals and long-term plans and activities of daily life (9). Therefore these disabilities will challenge people with MS disease, when they are attempting to pursue an active and compatible lifestyle (11). It seems that unpredictable courses of disease activity influence many different fields of the patient's life. Unpredictable periods can make severe feelings of helplessness and depression in patients with MS, while the hopelessness hypothesis states that unpredictable and negative events in the patient's life leads to depression (12). On the other hand, depression is an important predictor of psychological balance of MS patients (13), and studies have confirmed that there are relationships between structural brain le-

sions and depression in MS patients (12). There is a possibility that mental health status can change period of MS disease; as Charcot (1879), has discussed, grief and worry might influence onset and exacerbation of disease symptoms. Recent research has provided some evidence regarding the relationship between emotional states and disease activity in MS disease (9).

A variety of studies have confirmed the relationship between structural brain lesions in MS patients and depression (12). Measurement of depression in patients with MS is complicated because some of the symptoms are identical between depression and MS disease (sexual dysfunction, excessive fatigue, cognitive difficulties, psychomotor retardation, mood changes, sleep changes and emotional changes) (14). Patients with MS often hide symptoms of depression and they complain from other symptoms (15). Therefore, treatment plans for depression among MS patients should be treated with an individual and integrated approach (16). Currently there are no definitive treatment for MS disease and medications only reduce relapse rate, prolong remission, limit the onset of new MS lesions, and postpone the development of long-term disability (17). Nowadays the goal of all current and emerging therapeutic strategies for these patients is to return them to a normal life despite of their disease, and several therapies (modafinil, dalfampridine, baclofen, diazepam, gabapentin and opioids) have been used for symptomatic treatment of disability and symptoms, yet they do not improve disease outcome (17).

For managing the symptoms of MS disease and improving or maintaining function and preserving the patient's quality of life, careful clinical monitoring and pharmacologic and non-pharmacologic therapies are recommended (18). Complementary therapies (such as non-pharmacologic therapies) are widely used by MS patients, and progressive muscle relaxation therapy (PMRT) is a form of complementary therapy (19). The relaxation response is a physiological state and incompatible response against stress response (20). Muscle tension is usually associated with stress and anxiety, which are strongly related to depression. In fact, relaxation therapy is comprised of several methods that show patients how to achieve relaxation. Most programs include training special breathing and progressive muscle relaxation procedures (tension-release cycles) to reduce physical and mental tension (21).

PMRT was first identified by Jacobson in 1934 as a way for tensing and releasing 16 muscle groups. He stated that the mind and selected muscles work together in an integrated manner. Muscles and body can be relaxed or can be kept away from stress, anxiety and sympathetic activity with mental relaxation (22). Wolpe in 1948 adopted this technique for systematic desensitization therapy. Bernstein and Borkovec in 1973 adopted this technique for stress management in cognitive-behavioral therapy and they developed a shortened and modified form of the PMRT, and currently this form of relaxation therapy is being commonly used. Some of these adjustments are:

seven or four muscle groups, relaxation through recall, recall and counting, and counting (22, 23).

Previous studies have indicated that depression is prevalent in MS patients and affects treatment adherence and is associated with neurological damage that results from MS (24-42). Despite the high prevalence of depression in patients with MS and its severe impact on physical and mental health, nowadays there are no completely effective treatments for depression (5). There are significant results indicating the effectiveness of PMRT on the normal human brain and patients with MS and a brain lesion that suffer from depression; for example an investigation of 13 controlled studies on patients without brain lesions revealed that PMRT for depression treatment in different patients (such as, multiple somatoform syndrome, cancer disease, pulmonary disease, cardiac disease, muscular pain, tinnitus disease and night eating syndrome) is better than no treatment, placebo treatment, or other behavioral methods. Also follow-up (after several months) treatments were more effective than the first intervention (43-55). A few studies, have shown that PMRT is effective on quality of life, wellbeing and stress management, and this reduces symptoms such as pain, fatigue, anxiety and depression (9, 55-57).

2. Objectives

The aim of this study was to determine whether PMRT could reduce the level of major depressive disorder in female MS patients of the Shiraz Multiple Sclerosis Aid Society.

3. Materials and Methods

This study was an applied-experimental research with randomized controlled trial design plus pre and posttests. This study compared two groups; experimental and control, where the first group received PMRT and the second group did not receive any treatment for depression, respectively.

In spring 2010, from the 2800 MS patients of the Shiraz Multiple Sclerosis Aid Society (SHMSAS), 30 depressed female volunteers participated in relaxation therapy. They answered the questionnaire before the intervention. Criteria of MS and major depressive disorder (MDD) disease from minimal to severe were confirmed by the SHMSAS and BDI-II, and after the pretest they were randomly divided to two groups. The experimental group received standard care for MS disease plus 60 minutes of psychological intervention (PMRT) for each session (twice a week for six weeks) while the control group received only standard care for MS disease, and at completion the two groups cooperated again in the posttest.

Ethical considerations and rights were applied for this research (respect of the basic rights of patients such as, privacy, cultural and social values, freedom of choice and honesty about characteristics of therapy and therapist's competence). The cases of the two groups were matched

in terms of age, marital status, education and income. Selection criteria for inclusion and exclusion were as follows:

1- Agreement of the individual to participate in the research, 2- at least literacy for reading and writing, 3- physical ability to participate in therapy sessions, 4- doing homework daily at home, 5- filling notes every week, 6- not having any psychotic disorder, bipolar disorder (depressive episode) and major depressive disorder with psychotic features.

There was no drop out of patients during the intervention, and after treatment, patients of both groups answered the questionnaire for the second time.

3.1. Tools

In this study progressive muscle relaxation, method of Bernstein et al. (22), and also the Beck Depression Questionnaire (Beck, Epstein, Brown and Steer, 1988) were used, with the reliability and validity examined for the Iranian population (the validity of questionnaire was confirmed by the positive correlation between BDI-II and brief symptom inventory (BSI)); Pearson's coefficient was 0.87, and factor analysis (to determine underlying relationships between variables) showed three factors: physical, cognitive and affective. The reliability of the questionnaire using the method of internal consistency was 0.91 (Cronbach's alpha coefficient) (58).

The BDI-II was developed based on the criteria of diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) for diagnosing depressive disorders (59). The BDI-II is a brief scale that is acceptable for researchers in clinical observations and patient description. As a screening instrument, validity and capability of case-finding for this questionnaire has been proved. It is a subjective paper and pencil questionnaire with ordinal scale for depression as a qualitative variable. In addition cut-off points 0-13, 14-19, 20-28 and 29-63 indicate minimal, mild, moderate and severe depression (59).

3.2. Validity and Reliability

Content validity of the questionnaire was improved by rewording and adding items to assess DSM-IV criteria for depression. Also validity was confirmed by the positive correlation between Hamilton Depression Rating Scale, Edinburg Postnatal Depression Scale and the Hospital Anxiety, and Depression Scale-Depression, with a Pearson r of 0.62 to 0.81. The reliability of the questionnaire using retest coefficients and internal consistency was 0.93 (by Pearson's correlation) and 0.91 (by Cronbach's alpha coefficient) (59).

3.3. The Content of Therapy Sessions

The best way for muscle relaxation is for muscles to be contracted as much as possible, and then be relaxed suddenly (tension-release sequence). The released force from the treatment increases the excitability threshold. The released force is a big step toward deeper relaxation and patients can understand the feeling of tension and relaxation of muscles (comparative judgment). Relaxation therapy was divided to two parts:

1- The first six sessions: special breathing plus contraction and relaxation of muscles, with gradual reduction of the number of muscles involved.

2- The second six sessions: special breathing plus contraction and relaxation of mind (20).

3.4. Data Analysis Method

To eliminate uncontrolled variables (the effect of pre-test on the post-test) analysis of covariance was used (analysis of covariance eliminates the covariate variable). Also Levine Test was used for revealing the difference between the two groups. The experimental design of this study included the independent (PMRT) and dependent variable (depression), while analysis of variance used the method of repeated measures.

4. Results

Thirty patients participated in this study that were randomly divided in two groups (experimental and control). Tables 1 and 2 were designed for a glimpse to background variables and descriptive statistics of depression.

Table 1 reveals that most patients in this study were in their third decade of life and most of them had a bachelor's degree of education and single patients were more than others while half of them were sick for more than five years and they had experienced symptoms from mild to severe. Table 2 shows that all patients had depression and some of them had severe depression and in the experimental group the mean value indicates mild depression. The research hypothesis stated that, PMRT reduces depression level in MS patients and this hypothesis was checked by Tables 3,4 and 5.

Table 3, was designed to measure the equality of variances between groups. The results indicate that there was no significant difference in the variance of groups. The purpose of covariance analysis in Table 4 was to eliminate the covariate variable from the dependent variable and to estimate the central indexes. The results showed the mean and standard deviation had increased, by eliminating the impact of pre-test on the post-test and with considering the significance level. After the treatment of the experimental group, a significant reduction in depression variable occurred in seven levels. In Table 5, the impact of the independent variable on depression level was reviewed by analysis of variance with the repeated measures method.

Table 5 showed that the difference between pre-test and post-test was significant (P = 0.0001), indicating a 49% reduction in depression levels, which means that this reduction had occurred because of the relaxation therapy, with statistical power of 99%. The results of interaction depression and group showed significant increase effect in interaction weeks of treatment and group membership.

Table 1. Background Variables of the Two Groups (Experimental and Control) [a]

	Control	Experimental	Total
Age			
Second decade	4 (0.26)	5 (0.33)	9 (0.60)
Third decade	6 (0.40)	5 (0.33)	11 (0.73)
Fourth decade	3 (0.20)	4 (0.26)	7 (0.46)
Fifth decade	2 (0.13)	1 (0.60)	3 (0.20)
Education degree			
High school	4 (0.26)	3 (0.20)	7 (0.23)
Diploma	5 (0.33)	4 (0.26)	9 (0.30)
Bachelor	6 (0.40)	8 (0.53)	14 (0.46)
Master	0 (0.00)	0 (0.00)	0 (0.00)
Marital status			
Single	5 (0.33)	7 (0.46)	12 (0.40)
Married	6 (0.40)	5 (0.33)	11 (0.36)
Divorced	2 (0.13)	2 (0.13)	4 (0.13)
Widow	2 (0.13)	1 (0.60)	3 (0.10)
Sick precedent			
Less than 2 years	4 (0.26)	4 (0.26)	8 (0.26)
2 to 5 Years	3 (0.20)	2 (0.13)	5 (0.16)
5 to 10 Years	8 (0.53)	7 (0.46)	15 (0.50)
More than ten years	0 (0.00)	2 (0.13)	2 (0.60)

[a] Data are presented as No. (%).

Table 2. Descriptive Statistics of Depression Variables

	Control		Experimental		Total	
	Before	**After**	**Before**	**After**	**Before**	**After**
Mean	15.86	15.93	16.20	8.40	16.03	12.16
Median	13	13	16	5	14	10
Mode	11	10	11	5	11	5
Sum	238	239	243	126	481	365
Standard deviation	9.76	9.72	9.50	9.43	9.46	10.16
Variance	95.26	94.49	90.31	88.9	89.62	103.24
Range	31	31	36	40	37	40
Maximum	34	34	40	40	40	40

Table 3. Levine Test Results About Equal Variances in the Two Groups

Depression	F	First-Degree of Freedom	Second-Degree of Freedom	Significance Level
	0.463	1	28	0.502

Table 4. The Estimate of Average Depression Variable

Experimental Group	Average [a]	Number	Meaningful Level
Before intervention	16.08 ± 1.03	15	0.000
After intervention	8.24 ± 1.03	15	0.000

[a] Data are presented as Mean ± SD.

Table 5. Results of Variance Analysis with Repeated Measures Method

Source of Changes	Total Square	Mean Square	F	Significance	Effect	Statistical Power
Depression	224.26	224.26	27.46	0.0001	0.49	99
Interaction depression and group	232.06	232.06	28.41	0.0001	0.55	99
Error	228.66	8.16				

5. Discussion

Before treatment of MS disease, patients spent a lot of time trying to control their emotional disorders (like depression). Levels of depression in MS patients were studied by numerous researchers, and the results showed high levels of this complication and that the effects of depression on MS disease exacerbated (24-42). Through identifying and treating the first symptoms of depression, patients can increase their performance within the society.

This study was designed to assess a hypothesis derived from the Gate Theory; this theory states that psychological factors influence physical factors of pain, physical pain and psychological pain. This means that the same way stress and discomfort can exacerbate pain, relief and relaxation can also reduce pain (60). Depression is an overwhelming psychological pain (61), therefore this randomized controlled study was carried out, during 12 sessions, to determine the effects of a relaxation treatment on managing depression in patients with MS. The results showed that there was a significant relationship between treatment and depression. Table 4 shows mild depression in the experimental group and that after intervention there was a reduction of depression; more specifically, the results showed that patients in the experimental group indicated state of depression like normal people. Analysis of variance showed that these changes (49%) in the experimental group were a result of PMRT. Table 2 shows severe depression in some cases before and after treatment. These cases often hide symptoms of depression or can't recognize between symptoms of depression and MS disease. Also previous treatments (like pharmacologic therapy) for severe depression were continued. These cases took less advantage from this treatment.

The findings of this study showed that the level of depression (first symptoms of depression), was reduced even with short-term treatment, which was for six weeks (safe, inexpensive and effective intervention), and demonstrated the effectiveness of PMRT in reducing depression as an adjunctive and non-pharmacologic treatment (when treatment was used systematically). The findings of this short-term treatment were consistent with the research of Jorm et al. (21). They confirmed that PMRT, as a psychological intervention for depression, is more acceptable than other interventions (relaxation imagery and autogenic training). The findings of Schroder's study (29) demonstrated that both cognitive behavioral therapy (CBT) and PMRT appear to be effective treatments for depression in the normal human brain.

Based on the results of Sutherland et al. (9), Artemiadis et al. (55), Molina-Rueda and Pérez from Spain (56), and Ghafari et al. from Iran (57), potentially, it could be stated that PMRT may provide benefits, during different dimensions of the disease (vitality, fatigue and depression), for the brain affected by MS. However in psychological interventions, therapist training is essential. In fact, the relaxation technique is an acceptable psychological intervention, while it requires less skill and training than other techniques.

Finally, rationale and supporting evidence, and techniques used in PMRT are summarized in this article for intuitive understanding of future researchers about influences of PMRT.

PMRT is an effective treatment for depression in MS patients, although more studies should be done for investigating relaxation therapy as a first-line treatment in a stepped care approach to manage depression in patients with MS. Therefore, to obtain more accurate results, the following recommendations are suggested:

1- It is suggested that future studies, should use more objective clinical and laboratory results.

2- More control of confounding variables can reduce the limitations of the study (such as: sex, social and cultural status and disease progression).

3- Quantity of therapy will be better by using tapes, movies or booklets and long-term treatment.

4- Finally, screening programs are recommended to detect depression in patients with MS to facilitate access to services.

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Author's Contributions

Seyyedeh Zahra Safi conceived and designed the study, collected and interpreted the data, performed the statistical analysis, drafted and revised the manuscript, and approved the final version of the manuscript.

Declaration of Interest

None.

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