Research Paper: The Effect of an Eight-week Pilates Training on Interleukine-18 Level, Fatigue, and Balance in Women With Multiple Sclerosis

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ABSTRACT

Background: Proinflammatory cytokines increasingly cause inflammation in patients with Multiple Sclerosis (MS). In this regard, the current study aimed to shed light on the effectiveness of an eight-week Pilates training program in the level of interleukin-18, the severity of fatigue, balance, and physical disability, in females with MS.

Methods: This study was a quasi-experimental research with a pre-test-post-test design and a control group and conducted in Sirjan City, Iran. A total of 30 female MS patients (Mean±SD age: 30.15±6.97 years; 2≤ expanded disability status scale≤5.5) were selected using a purposeful sampling method and divided into control and experimental groups. The experimental group conducted the Pilates exercises for eight weeks, three sessions per week (lasting 45-60 minutes), while the control group had no regular physical activity. Before and after the training program, we evaluated fatigue, physical disability, and balance using the fatigue severity scale, the expanded disability status scale, and the Berg balance scale, respectively. Also, 5 mL of blood was taken from each participant to evaluate the interleukin-18 level. Then, the independent t-test was used to compare the pretest-posttest scores.

Results: The findings indicated that the Pilates training program significantly decreased the level of interleukin-18, the severity of fatigue, and the score of physical disability (P≤0.05), and increased the balance (P≤0.05), in females with MS.

Conclusion: Therefore, patients with MS can make the best use of such exercises to strengthen their immune systems and performances.

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1. Introduction

Multiple sclerosis (MS) develops following a disturbance in the balance of anti-inflammatory and proinflammatory cytokines and continues through the deterioration of myelin sheath [1]. Cytokines are among the most significant products of the immune response [2] and play an important part in the development of various inflammatory processes [3]. In healthy people, there is a balance between the helper T-cell type 1 (Th1) proinflammatory cytokines and the helper T-cell type 2 (Th2) anti-inflammatory cytokines; the specified balance deviates towards the proinflammatory cytokines in patients with MS. Also, in organ-specific autoimmune diseases, such as MS the Th1 behaves through the release of interferon-γ and causes inflammatory reactions by the immune system or intensifies delayed sensitivity [4, 5].

The interferon-γ and interleukin (IL)-18 can be found in the brain, cerebrospinal fluid, and the peripheral cells of MS patients, particularly in the acute stage of disease [6]. The IL-18 is a proinflammatory cytokine to produce sequential inflammatory procedures [7]. Thus, inflammatory elements, such as caspase-1 and IL-18 can exacerbate the inflammatory microglia and astrogliosis, leading to demyelination and subsequently increased oligodendrocyte elimination [8]. Since IL-18 can generate interferon-γ, it can cause exaggerated responses that nearly damage the body [9]. Thus, blocking the IL-18 activity is presumed to be an interesting therapeutic target in autoimmune diseases. Also, myelin/axonal damage is associated with the main symptoms of MS, including fatigue, imbalance, and physical disability [10].

Fatigue has been considered as the most common complication of MS and can lead to insufficient daily living and lower quality of life. This side effect is also prevalent in 80% of patients, nearly 70% of whom had impaired quality of life [11]. The four primary mechanisms that cause the pathophysiological fatigue in MS include structural damage to white and gray matter, inflammatory procedures, a network of incompatibilities resulting in structural damage or inflammation, and sensitive cognitive states [12].

Imbalance is another MS complication. Balancing and posture control issues are prevalent in MS patients and can decrease functional autonomy, boost disability, and increase the likelihood of falling. Physical disabilities and the fear of falling along with elevated stress concentrations may be observed in such patients [13]. Moreover, the quantity of motor disability was further acknowledged as the most critical symptom, from the perspective of MS patients [14]. In this respect, myelin sheath damage disturbs the transfer of nerve impulses from the brain to the muscles, therefore, some parts of the muscles gradually lose their ability [15].

The interventions of exercise and behavioral change can modulate the motor disability and enhance the psychological functioning, in MS patients [10]. Besides, regular physical activity can modulate the release of anti-inflammatory and proinflammatory cytokines and provide desirable immune system responses to reduce or deter demyelination and axonal loss [4]. By increasing caspase-1, an eight-week regular exercise program modulated the release of proinflammatory cytokines, such as IL-18 and IL-1β from macrophages [16]. Also, 12 weeks of a moderate-level resistance training program significantly mitigated the serum levels of IL-18 and C-reactive protein, in old males [17].

Concerning the impact of exercise on fatigue, balance, and physical disability, further studies were performed in various areas. For example, six weeks of Pilates exercises mitigated fatigue and depression and subsequently improved the quality of life in the experimental group, compared with the control group [18]. Also, Baquet et al. indicated that short-term aerobic exercises did not significantly impact the quality of life and fatigue, in MS patients [19]. However, six weeks of Pilates exercises have significantly affected the balance of females with MS [20]. Learmonth et al. examined the combined effect of practice on balance; they reported no significant enhancement in the balance of the experimental group, compared with the control group [21].

Currently, the Pilates exercises attract physiotherapists' attention. As these exercises can be done in a reclined state with no tolerance of weight, they can help patients [13]. Therefore, Pilates is presumed as an appropriate technique for practicing mind-body awareness and controlling situational motions through greater nerve and muscle uses [22].

Concerning the values and functions of the Pilates exercises, and given that suitable physical activities reduce the levels of inflammatory markers, it seems that the use of the Pilates exercises is an appropriate intervention for MS patients. However, no research has been carried out on the effectiveness of Pilates or other types of exercises. Therefore, the present research primarily aimed to determine the impact of an eight-week Pilates training

program on the level of IL-18, the severity of fatigue, balance, and physical disability, in females with MS.

2. Methods

Study design

The current study was a quasi-experimental research with applied methodology. Also, the research population consisted of 400 members of the National Multiple Sclerosis Society of Sirjan City, Iran, in 2017. In this research, sports medical screening examinations were conducted and the participants received interventions. Besides, informed consent was essential for participants to be included in the research. Based on the previous research, a purposeful sampling method was used to select 30 females with MS (age range, 20 to 40 years; 2≤expanded disability status scale≤5.5).

The inclusion criteria were at least one-year diagnosis of MS, the absence of other diseases (cardiovascular, respiratory, skin, etc.), the age range of 20 to 40 years, and no recurrence of the disease within two months of the outset of the research. The exclusion criteria included the irregular participation of the subjects in the training sessions (ie, the absence of more than three sessions led to the participant's removal), the exacerbation of the disease during the research, and excessive fatigue. Finally, 30 subjects were randomly assigned to the control group (n=15) and experimental group (n=15). Furthermore, both groups received medications during the research.

Procedures

Initially, height, weight with minimal clothing, and Body Mass Index (BMI) were evaluated using Seca height measure, Tanita SC-240 body composition monitor, and the formula of body weight divided by height square, respectively [23].

Blood samples were taken from the subjects, in two phases (two days before the beginning of Pilates exercises and two days after their completion). After five minutes of rest, 5 mL of venous blood was taken in the morning and immediately added to tubes containing ethylenediaminetetraacetic acid. The blood samples were maintained at -20oC until assay. Then, blood supernatant was collected by 15 minutes of centrifugation and analyzed using Enzyme-linked Immunosorbent Assay (ELISA). During the tests, the serum was melted and the concentration of IL-18 serum levels (IL-18 human kit Busters sample made in the USA; detecting range, 156-1000 pg/mL; sensitivity, 1 pg/mL; and ELISA based on kit instruction) was determined in each group. To control the impact of nutrition, the subjects were asked to refrain from foods and drinks, physical activity, alcohol, and caffeine use, since 12 hours before the blood sampling. The participants were also asked not to alter their diet during the research. Furthermore, there was a 48-hour interval between the injection of immunosuppressive drugs and blood sampling to regulate the drugs' impact on the examined immunological variables. All tests were conducted in a laboratory for medical diagnosis, in Sirjan, Iran.

Measures

Fatigue severity scale

This questionnaire was developed by Krupp et al., in 1989. Azamiyan et al. [24] confirmed the validity and reliability of the Persian version of the questionnaire. The fatigue severity scale is one of the most validated scales for the evaluation of fatigue in MS patients. It includes nine items graded from 0 (no fatigue) to 7 (severe fatigue). The patient's fatigue severity can be achieved by calculating the total scores of the items.

Berg balance scale

The Berg balance scale is a measurement of performance based on static and dynamic balance. It consists of 14 items; the total score varies from 0 to 56 (ie, the maximum score, showing a better balance) [18]. Also, each item includes five options scored from 0 to 4. Kashani et al. [23] verified the validity and reliability of the Persian version of this scale. Accordingly, the balance score is calculated by summing the scores of the 14 items and interpreted as follows: the scores range of 0 to 20, 21 to 40, and 41 to 56 represent high, moderate, and low risk of falling, respectively.

Expanded Disability Status Scale (EDSS)

EDSS was developed by Kurtzke to assess the severity of the disability. In this study, the diagnostic criteria for MS were obtained from the neurological examinations, magnetic resonance imaging, and EDSS by a neurologist. A portion of the damage to the central nervous system is assessed based on disability deterioration and disability status measurement. In other words, the damage is assessed based on modifications in EDSS results, which may represent the other aspects of the disease's incomplete developments, such as fatigue and decreased cognition [25, 26]. The EDSS score can also assist to identify performance and disability in a range of body activities, such as the participation of the nervous system.

The total score of EDSS varies from 0 (representing ordinary nerve functions) to 10 (representing nerve death that leads to MS). Thus, the higher the damage amount, the higher the score obtained. For instance, if the condition of the patients is on level 5, they can walk about 200 meters without any rest or help, while a patient with an EDSS score of 8 is essentially dependent on a wheelchair. Besides, the reduced EDSS scores imply enhancement in MS patients.

Interventions

The experimental group received the Pilates training exercises with low to moderate intensity, for eight weeks, three sessions per week. Each session lasted 45 to 60 minutes, and the exercises were conducted with 10 to 15 repetitions in three sets. Moreover, simple stretching movements were performed for 10 minutes in each session to warm up. Then, the main exercises of the training program, including stretches, energy movements, nerve-muscle coordination, and balancing were conducted. For the last 10 minutes, simple stretches were performed again to cool down. The main exercises included shoulder bridge, single-leg stretches, double-leg stretches, single-leg stretches with upper body rotation, the hundreds of movements, single-leg circles, single-leg bends, Cobra pose, darts, stars, aerobic movements, etc.

The exercises were set on four levels to regulate the intensity: In the initial sessions, the participants started the exercises at level 4 with no tools, then, they reached level 3 with enhanced patient results within the second week, also, within the last two weeks, they reached level 2 in some exercises. The assigned exercises were gradually advanced with more complicated exercises, the enhanced number of movements, and the use of facilities like balls and bands (in intermittent sessions). The control group did not do any exercises during this time and only finished the pre-test and post-test. Before the participants fulfilled the consent form, all issues related to different-test levels were fully clarified to them; they were ensured that their data would stay confidential and that the findings of the research would be reported in general.

Data analysis

The data were analyzed at two levels of descriptive (mean, standard deviation, and range) and inferential statistics. First, the Kolmogorov-Smirnov test was used to monitor the normal distribution of the data, in each group. The paired t-test and independent t-test were used for intragroup and intergroup comparisons, respectively. After ensuring the normal distribution of data, the data were evaluated using the SPSS. The significance level of 0.05 was regarded in all cases.

3. Results

At the beginning of the research, the subjects in both groups showed no statistically significant difference in age, height, weight, and BMI and both groups were homogeneous (Table 1).

Normal distribution of data

All the variables measured in this research were monitored for outbound data. The data for the factors of fatigue, balance, physical disability, and IL-18 level were normally distributed, based on the results of the Kolmogorov-Smirnov test with the significance level of 0.05. Therefore, the parametric tests could be used for data analysis. The P-values must be higher than 0.05 in the Kolmogorov-Smirnov test to demonstrate the normal distribution of the data, ie, the results of this test must be statistically insignificant. Since the test results were not statistically significant in both groups, the data were normally distributed. Table 2 presents the results of the given test.

Table 1. Comparison of the Demographic Characteristics of the Experimental and Control Groups Before Intervention (n=15)

Demographic Characteristics	Mean±SD		P
	Experimental	Control	
	Pre-test	Post-test	
Age (year)	32.10±13	33.9±6	0.39
Height (cm)	157.7±29	159.7±80	0.46
Weight (kg)	62.51±0.61	64.8±47	0.66
BMI (kg/m^2)	25.2412±0.1	25.2±3.20	0.81

Table 2. Kolmogorov-smirnov test results for the normal distribution of data in experimental and control groups

Variable	Groups	Control		Experimental	
		Statistic	P	Statistic	P
IL-18 (pg/mL)	Pre-test	0.715	0.687	0.63	0.822
	Post-test	0.633	0.818	0.53	0.941
Fatigue	Pre-test	0.939	0.341	0.409	0.996
	Post-test	0.806	0.535	0.86	0.541
Physical disability	Pre-test	0.506	0.96	0.658	0.779
	Post-test	0.57	0.902	0.812	0.525
Balance	Pre-test	0.684	0.837	0.665	0.768
	Post-test	0.473	0.979	0.686	0.735

After eight weeks of the Pilates exercises, the results of the paired t-test showed the P value of 0.001 (less than 0.05) for IL-18, fatigue, and physical disability in the experimental group (Table 3). It implies that the pre-test-post-test mean difference is significant in the experimental group. In other words, providing the independent variable (the Pilates exercises) has significantly decreased IL-18, fatigue, and physical disability, in the experimental group. However, the P values observed in the test of the control group for IL-18, fatigue, and physical disability were 0.064, 0.498, and 0.056 (higher than 0.05), respectively, implying that the pre-test, post-test mean difference was not significant in this group.

Also, the results of the independent t-test proposed that the P values observed for IL-18, fatigue, and physical disability were 0.001 (less than 0.05), which meant that the mean difference between pre-test and post-test was significant in both groups. Also, the mean difference between pre-test and post-test was higher in the experimental group than in the control group. In other words, the provision of the independent variable (the Pilates exercises) has significantly impacted the level of IL-18 reduction, fatigue severity, and physical disability in the experimental group.

Table 3. Comparison of the intragroup and intergroup changes in il-18, fatigue, physical disability, and balance

Variable	Groups	Mean±SD		Paired t-test			Independent t-test	
		Pre-test	Post-test	Pre-test, post-test Mean Difference	Intragroup	P	Intergroup	P
IL-18 (pg/mL)	Control	332.67±81.19	327.3±79.3	5.33	2.01	0.064	-7.673	0.001
	Experimental	339.3±67.6	272.3±65.73	61.33	7.23	0.001		
Fatigue	Control	5.423±0.719	5.354±0.828	0.07	0.696	0.498	-5.682	0.001
	Experimental	5.062±0.948	3.474±1.04	1.59	6.40	0.001		
Physical disability	Control	1.098±0.49	1.072±0.47	0.026	2.09	0.056	-8.347	0.001
	Experimental	1.21±0.36	0.73±0.37	0.48	7.52	0.001		
Balance	Control	26.87±9.66	27.53±9.64	-0.66	-2.092	0.055	10.53	0.001
	Experimental	28.6±09.03	37.07±7.59	-8.46	-12.67	0.001		

After eight weeks of the Pilates exercises, the results of the paired t-test for balance revealed the P-value of 0.001 (less than 0.05), in the experimental group (Table 3). Thus, the pre-test-post-test mean difference was significant in this group. In other words, providing the independent variable (the Pilates exercises) has significantly increased the balance in the experimental group. However, the P-value in the test of the control group was 0.055 (higher than 0.05), suggesting that the pre-test-post-test mean difference was not significant, in both groups.

Moreover, independent t-test results for balance showed the P-value of 0.001 (less than 0.05), indicating that the pre-test, post-test mean difference was significant in both groups. Also, the pre-test-post-test mean difference was higher in the experimental group than in the control group. In other words, the provision of the independent variable (the Pilates exercises) has significantly enhanced the balance in the experimental group.

4. Discussion

This study showed that an eight-week Pilates training program significantly decreased the serum levels of IL-18, in women with MS. This result is consistent with the findings of Kabir et al. and Christiansen et al. [27, 28].

No research investigated the effect of the Pilates exercises on cytokines, particularly IL-18, in MS patients. However, Christiansen et al. found that twelve-week exercises significantly reduced the IL-18, in obese subjects [28]. Also, Ali Nejad et al. In a study showed that combined exercise reduces interleukin 18 in inactive girls [27]. The same level of practice is one of the possible reasons for this research to agree.

Contrarily, Hoseini et al. documented a significant difference in the levels of IL-18, fasting glucose, insulin, and insulin resistance, in athlete and nonathlete military personnel [29]. The discrepancy between the results of these studies may be caused by the different study samples, exercise durations, and the intensity of exercises. Also, there was no balance between inflammatory Th1 cytokines and anti-inflammatory Th2 cytokines in patients with MS. Moreover, most therapies rely on the study of the Th1 and Th2 cytokines ratio.

As the readiness levels and physical activity are associated with cytokine semicircles and the status of the immune system, regular physical activity can be active in disease progression by affecting the immune system [30]. Exercise is generally marked by anti-inflammatory effects and may minimize proinflammatory cytokines [31-33]. Therefore, exercise-induced stimulation can significantly improve the cytokine balance and MS activity. In this analysis, cytokine reduction resulting from workouts was likely to have decreased Il-18. Considering the above-mentioned findings, it was hypothesized that routine and moderate-intensity exercises can reduce the IL-18 levels, however, further studies are needed to establish how exercises can cause changes in the course of the disease.

Consistent with the results of Akbas as well as Salehi et al. [18, 34], the eight-week Pilates training program significantly decreased the frequency of fatigue in the experimental group, compared with the control group. It also reduced the frequency of fatigue and improved the quality of life [18]. Salehi et al. showed a significant reduction in fatigue after an eight-week Pilates training program, three days per week, in 60-minute sessions [34]. Duration and the number of sessions could explain this reliability. The results of this study were inconsistent with that of Baquet et al. [19].

They found no significant effect of the treatments on the quality of life, frequency of fatigue, and depression, in patients with MS. The smaller sample size and lower exercise intensity could be the reasons behind the non-significant results in the study in question [19]. Besides, the pathophysiology of fatigue is not understood in MS patients; further studies are needed to explore the causes of fatigue and its descending trend following the training programs. Nevertheless, researchers found that increased body metabolism during and after workouts may explain the improved fatigue [10].

Also, the results of this study showed that the eight-week Pilates training program significantly increased the balance in the experimental group, compared with the control group. This result is consistent with the findings of Salehzadeh et al. and Ylva et al. [13, 35]. In the study of Salehzadeh et al., the experimental group completed an eight-week Pilates training program, three days a week, 60 minutes per session, while the control group only did daily living activities. The results indicated that the Pilates training program significantly changed the balance in the experimental group, compared with the control group [13].

However, Ylva et al. found that a seven-week balance exercise program decreased falling in patients with MS [35]. In the present study, the Pilates exercises impaired balance in these patients. Nonetheless, the results of this study contrasted with the findings of Kileff et al.; they reported no impact of physical activity on balance in individuals with MS [36]. The explanation for this inconsistency could be related to the early stages of the disease,

the amount of lesion, the duration of exercises, and the type of training programs. Consequently, the involvement of the pathophysiological mechanism of the brain volume reduction arising at the later stages of MS can be considered as a prognosis of impairment and cognitive decline [37]. In this regard, numerous studies indicated that exercise training can improve balance or prevent a decreased balance in MS patients. Muscle weakness and the loss of balance are also common in these patients. Practicing medical exercises with Pilates, based on central stability can change the body posture, suggesting a significant reduction in fat percentage as an active balance and movement tissue [38].

The results of this study showed that the eight-week Pilates training program significantly reduced physical disability in the experimental group, compared with the control group. This result is consistent with the findings of Shahrokhian et al. and Medina-Perez et al. [39, 40]. Shahrokhian et al. studied 30 female patients with MS, using an eight-week Pilates training program, three sessions a week, each session lasting 40 to 60 minutes. The Pilates exercises similarly improved the muscle endurance and strength in these patients [40].

Among the limitations of this research are the psychological distress and family problems in participants, the duration of the disease, the lack of cooperation with other subjects, the presence of illnesses other than MS (such as diabetes, cardiovascular disease, asthma, epilepsy, skin problems, arthritis, breathing problems, psychological distress, mental disorders, etc.), difficulty in commuting to the gym, and the lack of fat measurement. According to the study results, it is recommended to use the Pilates training programs as beneficial and supportive therapies. Such exercises are cost-effective and have no negative side effects, also, they can reduce cytokine levels (ie, IL-18), mitigate the severity of fatigue, enhance the physical disability, and increase the health of patients with MS. Future studies should examine the impact of the Pilates exercises on patients with MS, using other inflammatory factors, such as IL-4, -10, and -17, as well as other functional factors.

5. Conclusion

According to the results of this study, the use of the Pilates exercises can reduce inflammatory markers, develop balance, and enhance fatigue and physical disability. Also, patients with MS should be informed about the benefits of Pilates training programs, including decreased proinflammatory cytokines (ie, IL-18), fatigue, and physical disability, and improved equilibrium to strengthen their immune system and physical-mental functioning. Therefore, specialists are recommended to prescribe the Pilates exercises along with drug therapy as a complementary treatment.

Ethical Considerations

Compliance with ethical guidelines

The present study was approved by the Ethics Committee of Biomedical Research affiliated to Islamic Azad University, Isfahan (Khorasgan) Branch (Code No.: IR.IAU.KHUISF.REC.1396.35).

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Authors' contributions

Study design: Farzaneh Taghian; Data collection and analysis, manuscript preparation, reading and approving the final version of the manuscript: Both authors.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Reale M, de Angelis F, di Nicola M, Capello E, di Ioia M, Luca Gd, et al. Relation between pro-inflammatory cytokines and acetylcholine levels in relapsing-remitting multiple sclerosis patients. Int J Mol Sci. 2012; 13(10):12656-64. [DOI:10.3390/ijms131012656] [PMID] [PMCID]

[2] Zar A, Ebrahim Kh, Hovanloo F, Amani D. [Effects of an 8-week endurance training course on changes in interferon gamma and leukocyte subsets (Persian)]. J Isfahan Med Sch. 2012; 30(185):488-96. http://jims.mui.ac.ir/index.php/jims/article/view/1851

[3] Farhadi M, Tabatabaei A, Shekarabi M, Noorbakhsh S, Shokrollahi MR, Javadi Nia Sh, et al. [Inflammatory cytokine detection in adenotonsill and peripheral blood mononuclear cells- culture in adenotonsillectomy patients: A comparative study (Persian)]. Tehran Univ Med J. 2013, 71(1):31-6. http://tumj.tums.ac.ir/article-1-35-en.html

[4] Mokhtarzade M, Majdinasab N, Ranjbar R, Negaresh R. [The effect of regular physical activity on cytokine in people with multiple sclerosis: A systemic review (Persian)]. Sport Physiol. 2018; 10(37):99-122. [DOI:10.22089/SPJ.2018.1152]

[5] Pak F, Nafariyeh T, Asghari N, Shokrollahy M, Kokhaei P. [Immunopathology of multiple sclerosis (Persian)]. Koomesh. 2013; 14(2):117-29. http://koomeshjournal.semums.ac.ir/article-1-1604-en.html

[6] Kawayama T, Okamoto M, Imaoka H, Kato S, Young HA, Hoshino T. Interleukin-18 in pulmonary inflammatory diseases. J Interferon Cytokine Res. 2012; 32(10):443-9. [DOI:10.1089/jir.2012.0029] [PMID]

[7] Karakas Celik S, Öz ZS, Dursun A, Unal A, Emre U, Cicek S, et al. Interleukin 18 polymorphism is a risk factor for multiple sclerosis. Mol Biol Rep. 2014; 41(3):1653-8. [DOI:10.1007/s11033-013-3013-5] [PMID]

[8] Jha S, Srivastava SY, Brickey WJ, Iocca H, Toews A, Morrison JP, et al. The inflammasome sensor, NLRP3, regulates CNS inflammation and demyelination via caspase-1 and interleukin-18. J Neurosci. 2010; 30(47):15811-20. [DOI:10.1523/JNEUROSCI.4088-10.2010] [PMID] [PMCID]

[9] Wawrocki S, Druszczynska M, Kowalewicz-Kulbat M, Rudnicka W. Interleukin 18 (IL-18) as a target for immune intervention. Acta Biochim Pol. 2016; 63(1):59-63. [DOI:10.18388/abp.2015_1153] [PMID]

[10] Roshandelpour Z, Abedanzadeh R. [The effect of 12 weeks of training Pilates on balance and fatigue in women with multiple sclerosis (Persian)]. Navid No. 2018; 20(64):1-12. [DOI:10.22038/NNJ.2018.10575]

[11] Phyo AZZ, Demaneuf T, De Livera AM, Jelinek GA, Brown CR, Marck CH, et al. The efficacy of psychological interventions for managing fatigue in people with multiple sclerosis: A systematic review and meta-analysis. Front Neurol. 2018; 9:149. [DOI:10.3389/fneur.2018.00149] [PMID] [PMCID]

[12] Manjaly ZM, Harrison NA, Critchley HD, Do CT, Stefanics G, Wenderoth N, et al. Pathophysiological and cognitive mechanisms of fatigue in multiple sclerosis. J Neurol Neurosurg Psychiatry. 2019; 90(6):642-51. [DOI:10.1136/jnnp-2018-320050] [PMID] [PMCID]

[13] Salehzadeh K, Ayromlou H, Khajaiy S, Saberi Y. [Effects of Pilates on changes in balance, body composition, and vital signs including dual blood pressure and resting heart rate in females with multiple sclerosis in Tabriz, Iran (Persian)]. Iran J Nurs Res. 2018; 13(2):17-24. http://ijnr.ir/article-1-2018-en.html

[14] Khorshid Sokhangu M, Rahnama N, Etemadifar M, Rafeii M. [The effect of neuromuscular exercise on balance and motor function in woman with multiple sclerosis (Persian)]. Stud Med Sci. 2018; 29(5):362-71. http://umj.umsu.ac.ir/article-1-4375-en.html

[15] Freeman JA, Gear M, Pauli A, Cowan P, Finnigan C, Hunter H, et al. The effect of core stability training on balance and mobility in ambulant individuals with multiple sclerosis: A multi-centre series of single case studies. Mult Scler. 2010; 16(11):1377-84. [DOI:10.1177/1352458510378126] [PMID]

[16] Shirato K, Imaizumi K, Sakurai T, Ogasawara J, Ohno H, Kizaki T. Regular voluntary exercise potentiates interleukin-1β and interleukin-18 secretion by increasing caspase-1 expression in murine macrophages. Mediators Inflamm. 2017; 2017:9290416. [DOI:10.1155/2017/9290416] [PMID] [PMCID]

[17] Kabir B, Taghian F, Ghatreh Samani K. [Dose 12 week resistance training Influence IL-18 and CRP levels in elderly men? (Persian)]. Razi J Med Sci. 2018; 24(165):77-84. http://rjms.iums.ac.ir/article-1-3201-en.html

[18] Akbaş E, Ünver B. A six-week pilates exercise protocol for improving physical and mental health-related parameters. Malays J Mov Health Exerc. 2018; 7(2):65-79. https://www.researchgate.net/publication/326182942

[19] Baquet L, Hasselmann H, Patra S, Stellmann JP, Vettorazzi E, Engel AK, et al. Short-term interval aerobic exercise training does not improve memory functioning in relapsing-remitting multiple sclerosis - a randomized controlled trial. Peer J. 2018; 6:e6037. [DOI:10.7717/peerj.6037] [PMID] [PMCID]

[20] Farsi AR, Shahidian Akbar P, Vaez Mosavi MK, Jamshidi AA. [Effect of Pilates training based on core stability on balance and electromyography of women with multiple sclerosis (Persian)]. Sci J Rehabil Med. 2017; 6(3):165-73. [DOI:10.22037/JRM.2017.1100377]

[21] Learmonth YC, Paul L, Miller L, Mattison P, McFadyen AK. The effects of a 12-week leisure centre-based, group exercise intervention for people moderately affected with multiple sclerosis: A randomized controlled pilot study. Clin Rehabil. 2012; 26(7):579-93. [DOI:10.1177/0269215511423946] [PMID]

[22] Ali Zamani S, Ghasemi GA, Karimi A, Salehi H. [Pilates exercise effect on pain and general health of female patients with chronic low back pain (Persian)]. J Res Rehabil Sci. 2011; 7(1):95-103. http://jrrs.mui.ac.ir/index.php/jrrs/article/view/163/335

[23] Kashani V, Salmanzade MR, Bahrami L. [Determination of validity and reliability of the Persian version of the 9-item Berg balance scale in elderly people (Persian)]. Koomesh. 2018; 20(1):25-33. http://koomeshjournal.semums.ac.ir/article-1-3757-en.html

[24] Azimian M, Shahvarughi Farahani A, Dadkhah A, Fallahpour M, Karimlu M. Fatigue severity scale: The psychometric properties of the Persian-version in patients with multiple sclerosis. Res J Biol Sci. 2009; 4(9):974-7. http://medwelljournals.com/abstract/?doi=rjbsci.2009.974.977

[25] Riddle DL, Stratford PW. Interpreting validity indexes for diagnostic tests: An illustration using the Berg balance test. Phys Ther. 1999; 79(10):939-48. [DOI:10.1093/ptj/79.10.939] [PMID]

[26] Giovannoni G, Tomic D, Bright JR, Havrdová E. "No evident disease activity": The use of combined assessments in the management of patients with multiple sclerosis. Mult Scler. 2017; 23(9):1179-87. [DOI:10.1177/1352458517703193] [PMID] [PMCID]

[27] Agha Alinejad H, Mehrabani J, Ansari Dogahe R, Piri M. The influence of resistance, endurance, and combined resistance-endurance exercise training on interleukin-18 and c-reactive protein level in inactive female adolescents. Tabari J Prev Med Spring. 2016; 2(1):38-47. http://tbsrj.mazums.ac.ir/article-1-3516-en.html

[28] Christiansen T, Paulsen SK, Bruun JM, Pedersen SB, Richelsen B. Exercise training versus diet-induced weight-loss on metabolic risk factors and inflammatory markers in obese subjects: A 12-week randomized intervention study. Am J Physiol Endocrinol Metab. 2010; 298(4):E824-31. [DOI:10.1152/ajpendo.00574.2009] [PMID]

[29] Hoseini SA, Zar A, Amini M. [Comparison of the interleukin-18 levels and glycemic indices of athletic and nonathletic soldiers (Persian)]. Nurse Physician War. 2018; 6(18):33-40. http://npwjm.ajaums.ac.ir/article-1-508-en.html

[30] Passos GS, Poyares D, Santana MG, Teixeira AA, Lira FS, Youngstedt SD, et al. Exercise improves immune function, antidepressive response, and sleep quality in patients with chronic primary insomnia. Biomed Res Int. 2014; 2014:498961. [DOI:10.1155/2014/498961] [PMID] [PMCID]

[31] Golzari Z, Shabkhiz F, Soudi S, Kordi MR, Hashemi SM. Combined exercise training reduces IFN-γ and IL-17 levels in the plasma and the supernatant of peripheral blood mononuclear cells in women with multiple sclerosis. Int Immunopharmacol. 2010; 11(5):1415-9. [DOI:10.1016/j.intimp.2010.08.008] [PMID]

[32] Nunes RB, Alves JP, Kessler LP, Dal Lago P. Aerobic exercise improves the inflammatory profile correlated with cardiac remodeling and function in chronic heart failure rats. Clinics. 2013; 68(6):876-82. [DOI:10.6061/clinics/2013(06)24] [PMID] [PMCID]

[33] Castellano V, Patel DI, White LJ. Cytokine responses to acute and chronic exercise in multiple sclerosis. J Appl Physiol. 2008; 104(6):1697-702. [DOI:10.1152/japplphysiol.00954.2007] [PMID]

[34] Salehzadeh K, Ayromlou H, Khajei S, Saberi Y. [Effect of Pilates workouts on fatigue, motor disability and muscle flexibility in women suffering Multiple Sclerosis in Tabriz (Persian)]. J Health Promot Manage. 2017; 6(3):61-8. [DOI:10.21859/jhpm-07018]

[35] Nilsagård YE, von Koch LK, Nilsson M, Forsberg AS. Balance exercise program reduced falls in people with multiple sclerosis: A single-group, pre-test-post-test trial. Arch Phys Med Rehabil. 2014; 95(12):2428-34. [DOI:10.1016/j.apmr.2014.06.016] [PMID]

[36] Kileff J, Ashburn A. A pilot study of the effect of aerobic exercise on people with moderate disability multiple sclerosis. Clin Rehabil. 2005; 19(2):165-9. [DOI:10.1191/0269215505cr839oa] [PMID]

[37] De Stefano N, Airas L, Grigoriadis N, Mattle HP, O'Riordan J, Oreeja-Guevara C, et al. Clinical relevance of brain volume measures in multiple sclerosis. CNS Drugs. 2014; 28(2):147-56. [DOI:10.1007/s40263-014-0140-z] [PMID]

[38] Eftekhari E, Etemadifar M. Impact of clinical mat Pilates on body composition and functional indices in female patients with multiple sclerosis. Crescent J Med Biol Sci. 2018; 5(4):297-305. http://www.cjmb.org/uploads/pdf/pdf_CJMB_206.pdf

[39] Shahrokhian SH, Delaramnasab M. [Effect of Pilates exercises on improving the muscle function in women with multiple sclerosis (Persian)]. J Caspian Health Aging. 2017; 2(1):7-14. [DOI:10.22088/cjhaa.2.1.7]

[40] Medina-Perez C, de Souza-Teixeira F, Fernandez-Gonzalo R, de Paz-Fernandez JA. Effects of a resistance training program and subsequent detraining on muscle strength and muscle power in multiple sclerosis patients. NeuroRehabilitation. 2014; 34(3):523-30. [PMID]

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