Original Article

The effects of Combined Treadmill Training and Pharmacological Treatment on management of Multiple Sclerosis female patients

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Objectives: To compare the effectiveness of two treatment methods of 'combination pharmacological treatment and treadmill training' and 'pharmacological treatment' on management of multiple sclerosis (MS) female patients.

Methods: In this quasi experimental and interventional study a sample of 20 MS patients (mean age: 36.75 years) with Expanded Disability Status Scale scores (EDSS) 1.0 to 4.0 were randomly assigned to a 'pharmacologic treatment' (Ph) group and a combination group of 'pharmacologic treatment& treadmill training' (PhTT). All these individuals used the drugs of choice 'Rebif' and 'Avonex'. The intervention consisted of 8-weeks (24 sessions) of treadmill training (30 minutes each), at 40 - 75% of age-predicted maximum heart rate for the PhTT group. The Ph group followed their own routine treatment program. Balance, speed and endurance of walking, quality of life and fatigue were measured by Berg Balance Score, 10 meter timed walk test, 2 minute walk test, and Fatigue Severity Scale (FFS).Data were analyzed by paired t test and one way ANOVA.

Results: Comparison of results indicated that pre and post intervention led to significant improvements in the balance score (P=0.001), 10m walk time (P=0.001), walking endurance (P=0.007), and FFS (P=0.04) in the PhTT group. In contrast, no significant changes were observed in the Ph group's balance score, 10m timed walk and fatigue, while there was a significant decrease in the 2min walking distance (P=0.015) in this group.

Conclusion: These results suggest that treadmill training in combination with pharmacological treatment improve balance and walking capacity and level of fatigue in women with mild to moderate MS.

Keywords: multiple sclerosis, pharmacology, treadmill training, fatigue, ambulatory function.

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Introduction

MS is a degenerative inflammatory disease of the CNS, which may involve the brain, optic nerve and spinal cord (1). This auto-immune disease is a progressive demyelinating disease of the white matter of the CNS (2,3). The demyelination of the axons is associated with the many symptoms experienced by those with MS (4). Patients with MS exhibit various symptoms such as weakness, ataxia, increased reflex activity, spasticity, and sensory disturbances depending on the site of the pathological process in the CNS (5,6). With a prevalence rate of 110/100,000, MS is one of the most frequent neurological diseases (2) and affects approximately 1,000,000, individuals worldwide (7). MS begins slowly, usually in young adulthood, and continues throughout life, with periods of exacerbation and remission (8,9).

Patients with MS show a poor exercise tolerance, with fatigue and dyspnea on exertion that limits the activity of daily living (10). They present with a range of symptoms, but reduced mobility and fatigue are key problems, with up to 85% of people with MS reporting difficulty in walking (11). The ability to move may be affected by numerous impairments, including weakness, imbalance, fatigue, spasticity,

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and environmental conditions (12). Fatigue is also one of the major debilitating symptoms of MS and is thought to be due to a combination of central and peripheral changes. Centrally slowed axonal electrical conduction along motor pathways is thought to result in symptoms of fatigue. Peripheral changes include muscle fiber alterations and reduction in muscle cross-sectional area, and altered enzyme and metabolic activity (13). Quality of life is compromised in persons with MS and this is likely to be explained by several features of the disease, including an onset during the productive years of one's life, an uncertain and unstable disease course, diffuse effects throughout the CNS, and the absence of a cure (14). One of the primary aims of rehabilitation in people with MS is to maintain and improve functional independence (15).

On one hand, pharmacologic treatments are not effective in all MS patients. On the other hand, drugs have many side effects such as fatigue and psychological imbalance that intensify their complications. Hence, there is no well-known treatment that is completely effective (16). For example, regulators of the immune system and steroid therapy can reduce some symptoms of multiple sclerosis and are effective and widely used in patients. However, these drugs cannot stop the progression of the disease; they also have numerous side effects such as increased spasm, nausea, depression, nerve pain, fever and headache (17). Therefore, in recent years non-pharmacological methods known as complementary therapies have emerged. Complementary therapies are treatments of comprehensive nature that are used to provide patients with physical and mental comfort (18).

In the past, physicians had limited knowledge of their MS patients' physical activity, believing that fatigue and the overheating problems associated with the disease and patients' physical activity would aggravate the symptoms of MS(19). Recently, many researchers have demonstrated that standard physical therapy and other rehabilitative techniques may improve these functions to some extent, but they are not always successful (12). Literature review suggests that exercise therapy may be beneficial for patients with MS in terms of physical fitness, activities of daily living, and outcomes related to mood (1,20). Information on the response of MS patients to exercise with or without pharmacological treatments is limited, and study findings appear to be influenced by the level of physical impairment in study samples (21). In addition, the appropriateness of physical activity for people with MS largely depends on the patient's physiological tolerance and response to exercise (22). In a pilot study on people with MS, walking was well tolerated and the speed improved without increasing fatigue (23). Thus the purpose of this study was to evaluate the effectiveness of two treatment methods, 'combination of pharmacological treatment and treadmill training' and 'pharmacological treatment alone' on the management of MS patients. However, may we add that, a theory is not right or wrong in an absolute sense but judged to be more or less useful in solving the problems presented by patients (24).

Methods

In this quasi experimental and interventional study twenty women with MS (19-54years old) volunteered to participate in the study and obtained physician clearance prior to study enrolment. Subject inclusion criteria consisted of physician-diagnosed MS with a self-assessed 'Kurtzke Expanded Disability Status Scale' (EDSS) score of between 1 and 4.

All the subjects who were using MS disease-modifying drugs 'Rebif' and 'Avonex' were included and those using other drugs were excluded. Additionally, individuals were required to be able to walk on the treadmill with or without hand support. The subjects had not participated in physical activity for three months prior to the study. Individuals who were affected with cardiovascular disease, liver or kidney failure, symptomatic lung disease, diabetes, thyroid disorders, gout or orthopedic limitations were excluded. Pregnant and drug-abusing individuals (i.e. cigarette smokers or drug addicts) were also excluded. All subjects gave written informed consent to participate in the study. After completion of baseline evaluations, subjects were randomized to one of the two experimental groups: pharmacological treatment and treadmill training (PhTT) (test group), and pharmacological treatment (Ph) (control group). The participants' characteristics are presented in table (1).

Table 1. Characteristics of the 20 subjects with multiple sclerosis enrolled in the study

Variable	All Subjects (n=20)	PhTT group (n=10)	Ph group (n=10)	P
Age (year)	36.75(19-54)±9.00	36.80(24-54)±9.17	36.70(19-49)±9.32	0.98
Disease duration (year)	5.30(1-11)±3.11	5.60(2-11)±3.30	5.00(1-9)±3.05	0.67
EDSS score (0–10)	2.32(1-4)±1.21	2.40(1-4)±1.24	2.25(1-4)±1.25	0.79
Balance score	45.50(28-56)±7.92	46.50(35-56)±6.43	44.50(28-54)±9.43	0.58
Walking time (second)	8.89(6.19-12.24)±1.88	8.61(6.19-12.01)±1.94	9.16(6.62-12.01)±1.88	0.52
Walking distance (meter)	121.72(71-172)±24.20	121.95(89-146)±21.16	121.505(71-172)±27.73	0.96
FFS score	3.8(1-5.78)±1.53	3.38(1-5.33)±1.73	4.17(1.11-5.78)±1.28	0.25

P: *P* values assessed by one-way ANOVA

After medical history screening, participants were asked to complete the FFS (11,23) to assess the baseline level of fatigue. Balance and walking were evaluated as indicators of ambulatory function (13). Balance was assessed using the Berg Balance Scale(13,25).The 10 meter timed walk test(10-m TWT) and 2minute walk test (2-min WT) were conducted to evaluate walking speed and endurance, respectively (11,26).The time taken to walk 10meters over a straight walk path, and the distance travelled walking for 2minutes around a shuttle corridor track were recorded (11). Individuals were familiarized with the treadmill and all test protocols. All participants were assessed immediately prior to baseline and following the 8 week intervention.

Intervention program: The PhTT group subjects completed the supervised treadmill training (three sessions per week) exercises for eight consecutive weeks, in addition to their own treatment drug schedule. Each training session consisted of a 30 min walk on the treadmill (DKCity from China). The exercise class began and ended with about 10 min of stretching and flexion and rotation movements of the trunk and lower limbs. Training intensity was between 40-75% age-predicted maximal heart rate which was measured by a Sport Tester (Polar Electro OY type PE-3000 instrument from Finland).the Initial speed was based on baseline preferred walking speed and increased as selected by participants. To monitor exercise intensity, HR, time, speed and ratings of perceived exertion (RPE) were recorded using the modified 15-point Borg scale. The Ph group followed their own routine drug treatment program.

Data analysis: Pre-test data were examined at first reassessment for between group differences. Comparisons between pre and post-training measures of balance, walking speed and endurance and fatigue were analyzed using a paired t–test. Between-group differences of this study were examined using the one way ANOVA. Data were analyzed with SPSS version 16.0, using a significance level of p≤0.05.

Results

Ten MS women in the Ph group and ten MS women in the PhTT group took part in this study's test procedures. No exacerbations in their condition were reported during the eight-week training program.

As in table (1), there were no differences between the groups at baseline for either age, EDSS score, disease duration, balance score, walking time, walking distance, and FFS score (P>0.2, respectively). Balance score had improved significantly in the PhTT group (p<0.001) increasing from 46.50 (SD=6.43, range: 35-56) to 54 (SD=2.44, range: 50-56), whereas in the Ph group this score had reduced from 44.5(SD=9.43, range: 28-54) to 41.7 (SD=8.48, range: 28-54).This change however was not significant (P=0.07). When the effects of the treadmill training program were analyzed between these groups, the balance score of the PhTT group had significantly increased compared to that of the Ph group (P=0.00) after the intervention. Mean 10meterwalkingtime had decreased significantly in the PhTT group (p=0.00) from 8.61(SD=1.94, range: 6.19-12.01) to 7.01(SD=1.02, range: 5.84-8.45) seconds, but in the Ph group walking speed at baseline did not change significantly after eight weeks (p=0.14) and increased from 9.16 (SD=1.88, range: 6.62-12.01) to 9.47 (SD=1.92, range: 7-12.75) seconds.

Mean 2min walking distance had increased significantly in the PhTT group (p=0.00) from 121.95 (SD=21.16, range: 89-146) to 141.7 (SD=21.1, range: 116.5-184) meters, whereas the walking distance decreased significantly in the Ph group (p=0.01) from 121.50 (SD=27.73, range: 71-

172) to 110.40 (SD=23.11, range: 73-154) meters. The differences between the two groups were significant for the 10-m TWT and 2-min WT (p=0.00 respectively).

The FFS was used to assess the level of excessive fatigue before and after the eight week intervention. The average fatigue score at baseline was 3.38 (SD=1.73, range: 1-5.33) and decreased to 1.79 (SD=0.65, range: 1-2.88) in the PhTT group (P=0.00) and increased form 4.17 (SD=1.28, range: 1.11-5.78) to 4.23 (SD=1.04, range: 1.78-5.33) (P=0.82) following the eight week study in the Ph group. The analysis showed that differences between groups were significant for FFS score (]=0.00) (table 2).

Table 2. Pre intervention and post intervention values for balance, 10-m TWT, 2-min WT and Fatigue Scale Score in PhTT and Ph groups with multiple sclerosis

Variable	PhTT* group			Ph** group				
	Pre intervention	Post intervention	P^a	Pre intervention	Post intervention	P^a	F	P^b
Balance score	46.50(35-56)±6.43	54.00 (50-56)±2.44	0.00	44.50(28-54)±9.43	41.70(28-54)±8.48	0.07	25.25	0.00
Walking time (second)	8.61(6.19-12.01)±1.94	7.01(5.84-8.45)±1.02	0.00	9.16(6.62-12.01)±1.88	9.47(7-12.75)±1.92	0.14	22.27	0.00
Walking distance (meter)	121.95(89-146)±21.16	141.7 (116.5-184)±21.1	0.00	121.5 (71-172)±27.73	110.40(73-154)±23.11	0.01	21.05	0.00
FFS score	3.38(1-5.33)±1.73	1.79(1-2.88)±0.65	0.00	4.17(1.11-5.78)±1.28	4.23(1.78-5.33) ±1.04	0.82	11.98	0.00

P^a: P values assessed by paired t–test P^b: P values assessed by one-way ANOVA

*pharmacological and treadmill training intervention **pharmacological intervention

Discussion

According to the results of this study eight weeks of pharmacological treatment accompanied by treadmill training led to clinically significant changes in balance of patients with mild to moderate MS, whereas this factor had not changed significantly in the Ph group. DeBolt and McCubbin (2004) tested the effects of a resistance workout program on balance in MS patients. Unlike our finding, their results showed that balance did not change after 10weeks of training (27). In addition, Romberg et al did not find any change in balance after the 6 months exercise program (strength training and aquatic training) for MS patients with mild to moderate disability (EDSS 1.0 to 5.5)(28). But Giesser et al showed improvement in balance after 40 treadmill training sessions in MS individuals with severely impaired ambulation (EDSS 7.0 to 7.5) (29). Thus their study showed that treadmill training may bean appropriate exercise for balance improvement in MS individuals with severe ambulatory impairment. Muscle weakness is a hallmark symptom of MS and is associated with fatigue, reduced functional capacity and increased disability. Following the eight-week intervention, only the PhTT group showed significant improvement in both the 10-m TWT and the 2-min WT. These findings may be justified by the principle of specificity (30) of the training programs. Thus treadmill training is a specific practice and use of body systems concerned with walking (11, 31).

In Romberg et al's study, the duration of the 7.62m walk decreased by 12% relative to baseline after 6 months of exercise(27), whereas in this study the duration of the 10m timed walk was reduced by 18.58% with only 8weeks training. Also, according to Newman et al a 12% reduced mean 10m time was observed after 4weeks of treadmill training (11).

Increased endurance has positive implications for the lifestyle of individuals (32). The findings of the present study show that the mean 2min walk distance increased by 16.23% in the PhTT group, but decreased by 9.13% in the Ph group; this difference was statistically significant (P=0.015). Training appears to have benefited individuals by reducing the energy expenditure in walking, leading to energy savings. Even small savings in energy for those with more restricted mobility could be functionally important, allowing them to continue activity for longer periods of time (11). These same researchers reported that exercise significantly improved walking endurance (11,15,28,32,33). However, an individual who has poor balance due to MS will not be able to walk very well, thus with reference to the results of this study increased balance, leads to improved ambulatory function in test group participants.

Fatigue is one of the symptoms most frequently reported by MS patients, sometimes a predominant symptom at the onset of MS or associated with other neurological disorders (22). The results of the present study showed that treadmill training led to a significant decrease in the PhTT group's(test subjects) FFS score (47.04%).on the contrary, in the Ph group (control subjects) FFS score, increased by 1.41% after the 8weeksstudy. However, the results of the exercise training program in this study did not show similar outcomes to other reported results for exercise training programs (11,15,32). In contrast, some studies reported that various types of exercises can be useful introducing fatigue in MS individuals (1,34). Surakka et al. found that 6 months of aerobic and strength exercises resulted in reduced fatigue in women, but not in men (35).

Conclusion

The findings of the present study show that treadmill training accompanied by pharmacological treatment led to clinically significant balance improvement, level of fatigue reduction and increased mean speed in patients with mild to moderate MS.

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