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Effects of whole body vibration on hormonal & functional indices in patients with multiple sclerosis

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***Background & objectives*: Multiple sclerosis (MS) is a neurodegenerative disease, which affects the patients' mobility, and exercise training is considered to be beneficial for these patients. The aim of this study was to determine the effects of 10 wk of low intensity exercise and whole body vibration (WBV) training on fatigue, quality of life, functional and physical indices, and serum levels of ghrelin, leptin, and testosterone in MS patients.**

***Methods*: Thirty four MS patients with mild to moderate disability were recruited and randomly divided into two groups, the training group (n=17) and control group (n=17). Patients in the training group did low intensity exercise and WBV training programme three times a week for 10 wk. The control group continued their routine life. Intended variables like expanded disability status scale (EDSS), fatigue, quality of life, functional and physical indices consisted of balance, walking speed, functional mobility, functional muscle endurance, and walking endurance, and serum levels of ghrelin, leptin, and testosterone were measured before and after the protocol.**

***Results*: Thirty subjects completed the study (23 females, 7 males; mean age =38.80 ± 9.50 yr). Statistical analysis demonstrated that EDSS in the WBV training group was significantly decreased (*P*=0.01), balance (*P*=0.01), and walking endurance significantly increased (*P*=0.01) in MS patients (*P*<0.05).**

***Interpretation & conclusions*: The results suggest that low intensity exercise and WBV training have some beneficial impact on functional and physical indices of MS patients.**

Key words Hormone - multiple sclerosis - quality of life - whole body vibration

Exercise is beneficial for multiple sclerosis (MS) patients, especially on fatigue which is related to quality of life (QoL), as compared with a neurological rehabilitation protocol in subjects with mild to moderate disability[1,2]. Whole-body vibration (WBV) as a training method causes rapid contraction and relaxation in the muscles and is based on the mechanical multi-dimensional oscillations of muscle-nervous system[3]. The WBV increases the flow of blood, and lymphatic flow through the body[3], and can also increase the force of muscles in the short duration of time with less fatigue[4], which may improve some aspects of postural

control in individuals with disability or impaired vision[5]. Schuhfried *et al*[6] have demonstrated that WBV may have a positive effect on postural control and mobility in MS patients, and van Nes and colleagues[7] have found WBV as more effective on spasticity, muscle strength and motor performance in adults with stroke by comparing WBV with resistance training.

One of the most common complications of MS is the sedentary lifestyle which is due to changes in body composition, decrease muscle mass, and increase fat mass[1]. Changes in adipose tissue also affect leptin secretion. Leptin concentrations correlated positively with expression in subcutaneous fat, and leptin expression was also correlated with BMI[8]. Ghrelin modulates energy stores and expenditure in the adipocytes[6]. Ghrelin gene expression has been detected in subcutaneous and visceral adipose tissue[8]. There are evidences that suggest certain hormones like leptin and ghrelin (natural antagonists of leptin) are involved in the pathogenesis of MS and also regulate food intake, energy expenditure and metabolism[9].

Changes in hormonal concentrations in humans and rats have been described after WBV training[10,11]. Moreover, a role for testosterone has been proposed in the pathophysiology of MS[10], so it would be useful to determine the hormonal changes during WBV and their contributions to clinical response in MS patients. This study was designed to determine the effects of WBV training on expanded disability status scale (EDSS), fatigue, quality of life, functional and physical indices consisting of balance, walking speed, functional mobility, functional muscle endurance, and walking endurance and serum levels of ghrelin, leptin, and testosterone in MS patients.

Material & Methods

This study was conducted between February 2010 and February 2011 under the auspices of the Isfahan University of Medical Sciences, Alzahra Multiple Sclerosis Clinic (AMSC), Isfahan, Iran. The study protocol was approved by the Local Ethics Committee affiliated to the Isfahan University of Medical Sciences, Iran.

The study design was randomized controlled trial. Thirty four patients attending AMSC (age: 38.76 ± 9.66 yr, height: 162.00 ± 0.07 cm, weight: 62.38 ± 8.71 kg, BMI: 23.53 ± 3.34 kg/m^2 , EDSS; 3.11± 0.99) with definite MS according to McDonald's criteria[12], with relapsing- remitting (RR) form of the disease and EDSS 1.5-5 (from 40 patients as sample size) were enrolled in the study. The exclusion criteria included pregnancy, epilepsy, cancer, using prosthetic, diabetes, cardiovascular or pulmonary diseases, diplopia, and any type of orthopedic conditions including degenerative disc disease, back and spine conditions, arthritic conditions, degenerative hip or knee, paediatric injuries in hip, knee, and ankle, trauma, and osteoarthritis. All participants according to their sex were randomly assigned to a WBV training group (men=5, women=12) and a control group (men=4, women=13). Subjects in the experimental group participated in protocol of training for 10 wk. The control group continued their normal life, without adding physical activity to their lifestyle. Intended variables were measured during five days before starting the protocol as pretest and measured again 72 h after the end of the protocol. The weekdays of the test for each participant were the same. The time of blood sampling was between 0900 - 1200 h and each participant had specific times for blood sampling as pre- and post-test.

Variables consisted of EDSS, fatigue, quality of life, functional and physical indices including balance, walking speed, functional mobility, functional muscle endurance, and walking endurance. All tests of variables were done by the same investigator at the recording session of the post-tests who were blinded in the pre-tests. Peripheral blood samples were collected to determine the serum levels of ghrelin, leptin, and testosterone.

The training group completed supervised vibration training on the vibration platform for 10 consecutive weeks according to a progressive programme. Prior to testing, subjects were allowed to be familiar with the vibration procedures. The protocol of the training was designed with low intensity and gradually its intensity was increased. During the 10 wk training session each participant came for training three times a week with 48 h rest between each session. At the beginning of each training session the participants warmed-up by performing static stretching movements such as hamstring stretch, body twister, heel cord stretch, and quadriceps stretch, and then pedalling on a cycle ergometer for 5-10 min. The protocol of WBV (frequency and amplitude were set at 2-20 Hz and 2 mm, respectively) consisted of 15 sets of vibrations with three repetition. Duration of each set was one minute. Each participant stood on the vibration platform for 30 sec and consequently had rest for 30 sec. Between each set the patients had one minute to take rest. The breaks between the individual series were designed

to prevent rapid fatigue. After the eighth set, patients had a five- minute rest on chair. As the protocol was incremental, the duration of each set was 30 sec in the first week, and then reached to two minutes in the last week. The 15 sets consisted of squat [R-L (Right- Left) foot forward with a knee angle of 120)], deep squat (R-L foot forward with a knee angle of 90), lunge (R-L foot forward), sitting forward bend, modified press up position, one leg stance (R-L foot elevated), deep lunge (R-L foot forward), hip raise (R-L foot forward with a knee angle of 90) and calf massage. The participants maintained a static position on the platform while performing the above positions. The calf massage was performed in the last set of training. The control group continued their normal lifestyle without any training.

Measurements: Vital signs (such as temperature, blood pressure, and breath rate) before and after each training session were monitored to assure patients´ safety throughout the tests.

(i) Disability, fatigue, and quality of life - EDSS was determined by a neurologist who was blinded to this study. The Kurtz's EDSS is a method of quantifying disability in multiple sclerosis[12]. The presence and severity of fatigue were assessed by mean of the modified fatigue impact scale (MFIS)[13]. The Multiple Sclerosis Quality of Life-54 questionnaire (MSQOL-54) was used to assess health-related quality of life, which has been translated, culturally adapted and validated in an Iranian population[14].

(ii) Functional and physical indices - Berg balance scale was used to measure balance[15]. Functional reach was also used to measure the standing balance[16]. Timed 10-meters walk test (10 MWT) was used to evaluate gait speed[17]. The Timed up and go (TUG) test was used to assess the functional mobility[17]. The timed chair rise test was used to evaluate the local functional muscle endurance lower body extremity[17,18]. Modified press up position was used to assess upper body local functional muscle endurance[18]. The six minutes walk test (6MWT) measured the distance (in meters) walked within six minutes to assess an individual's walking endurance level[17].

(iii) Blood sample measurements - Venous blood samples (10 ml) were obtained from the antecubital vein of patients in a seated position. The serum samples were stored at -80°C for miximum 12 wk or until analysis. The concentrations of ghrelin, leptin, and testosterone were measured by enzyme immunoassay method[19].

Statistical analysis: Relevant statistical analyses were performed using SPSS version 15 (SPSS, Inc., Chicago, USA). Descriptive analyses were adopted for demographic and clinical characteristics reported as means ± SD. Before the statistical analysis Levene's test was used to show homogeneity of variances between the two groups before the start of the protocol. Kolmogorov-Smirnov test was used for determination of the normality of the distributions. Differences among groups were assessed by using analysis of covariate (ANCOVA).

Results

Thirty of the 34 patients recruited for the investigation completed the study and 16 of 17 in the study group completed the training programme sessions (Figure). Demographic and clinical characteristics are shown in Table I. There were no significant differences in baseline of age, weight, BMI, form of disease, disease duration, and EDSS between the two groups. The EDSS scores and fatigue scale score before and after 10 wk of protocol of training for both the groups are presented in Table II. The experimental group had 15.06 per cent significant (P<0.01) decrease in EDSS. After the training, the participants in the experimental group expressed no significant changes in the MFIS scores. Functional and physical indices are presented in Table III. Our results revealed significant improvement in

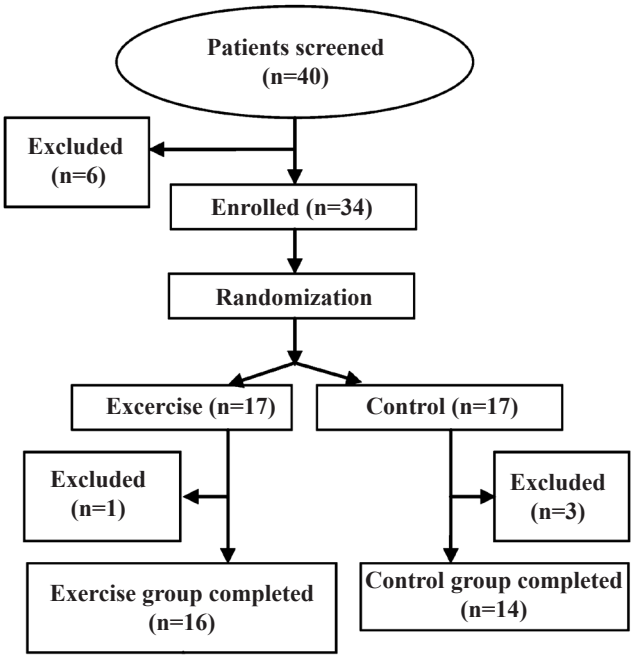

Figure. Study design flowchart.

Table I. Characteristics of the patients with multiple sclerosis (MS) who completed the study protocol and controls

Variable	All participants (n=30)	Exercise group (n=16)	Control group (n=14)
Gender			
Male N (%)	7 (23.3)	5 (31)	2 (14)
Female N (%)	23 (76.3)	11 (69)	12 (86)
Age (yr) (mean ± SD)	38.80 ± 9.50	37.06 ± 8.42	40.75 ± 10.56
Height (m) (mean ± SD)	1.62 ± 0.08	1.63 ± 0.08	1.61 ± 0.07
Weight (kg) (mean ± SD)	62.36 ± 9.21	63.68 ± 9.14	60.58 ± 9.40
BMI (kg/m^2) (mean ± SD)	23.53 ± 3.34	23.75 ± 3.48	23.27 ± 3.29
EDSS (mean ± SD)	3.11 ± 0.99	3.12 ± 1.19	3.10 ± 0.76
Disease duration (mean ± SD)	8.64 ± 5.7	6.5 ± 4.17	10.5 ± 6.4
Use of disease-modifying drugs	18	10	8
Disease course			
Relapsing - Remitting N (%)	30 (100)	16 (53.3)	14 (46.6)

BMI, body mass index; EDSS, expanded disability status scale

some of the variables of functional and physical indices like a significant increase in the balance (15.00%), and walking endurance (47.99%). Pre- and post-test mean values of experimental and control groups on all dimensions of the MSQOL-54 were adjusted in Table IV. There was no significant overall effect of training on quality of life. In addition, low intensity exercise and WBV training had not significantly changed the serum levels of leptin, ghrelin ghrelin/leptin ratio, testosterone, and testosterone/leptin ratio (P<0.05) (Table V).

Discussion

The results of this study indicated that unlike the control group, participants in the experimental group had significant decrease in EDSS and in some variables of functional and physical indices that included significant increase in the balance and walking endurance.

Significant decrease in patients' EDSS was not in line with an earlier study[1] which showed no changes in the EDSS of patients after WBV training[1]. The result of our study showed WBV training had no significant decrease in fatigue in MS patients, which was similar to that shown by Alguacil Diego *et al*[20] who demonstrated vibrotherapy had no significant effect on fatigue in multiple sclerosis patients.

Our results also showed no significant change in the MSQOL-54 scores. Schyns *et al*[21] reported that whole body vibration had no significant effect on QoL as measured by MSIS-29, which was similar to what was observed in this study. Limited walking prevents MS patients from participating in family and social activities and is a major determinant of overall impairment in ambulatory MS patients[22]. However, Rampello *et al*[1] showed that aerobic training significantly increased the emotional well-being, energy, and health distress scores. The mechanism of action of these changes is not clear and may not be related directly to the training programmes or baseline physical ability of patients. Aerobic and strength exercise showed an effect on the quality of life in patients with mild multiple sclerosis and it could improve the well-being of the participants[23]. Both intervention programmes facilitate the patient's socialization, which in itself may have contributed to some of the beneficial effects. Moreover, it has been demonstrated that exercise may enhance psychological well-being via a strong placebo effect[24]. The improvement observed in the quality of life could be explained by several reasons including improving socialization and decreasing isolation, promoting well-being and improving self-esteem, preventing symptoms secondary to MS (muscle atrophy, joint contractions, pressure sores), maintaining or improving range of motion and flexibility of joints, and endurance potential, and muscle strength[23]. Variable results from different studies could be due to different methodologies used for training and different scales used for measuring QoL. Moreover, factors like culture, and economic conditions may also contribute to quality of life and well-being of patients.

Table II. Before and after intervention values of expanded disability status scale (EDSS) and modified fatigue impact scale (MFIS) scores in patients

Variables	Exercise group (n=16)		Control group (n=14)		Levene's test	F	*P*	*η*	Observed power
	Before	After	Before	After					
EDSS	3.12 ± 1.19	2.65 ± 1.20	3.10 ± 0.76	3.03 ± 0.69	0.31	17.94	0.01	0.39	0.98
Physical S.	22.75 ± 6.73	20.06 ± 6.59	23.28 ± 5.83	23.42 ± 5.13	0.35	0.42	0.51	0.01	0.09
Cognitive S.	12.18 ± 7.8	13.12 ± 10.01	18.42 ± 8.97	18.71 ± 6.64	0.28	1.35	0.25	0.04	0.20
Psychosocial S.	4.75 ± 2.3	3.5 ± 2.47	5.38 ± 1.98	4.71 ± 2.43	0.77	0.10	0.74	0.00	0.06
MFIS	39.68 ± 13.5	37.18 ± 14.67	47.07 ± 14.56	46.85 ± 11.22	0.17	0.10	0.74	0.00	0.06

S, subscale; *P*, significance; *η*, partial eta-squared (demonstrated the changes of variable)
Observed power (to indicate an adequate number of subjects)
Values are mean ± SD

Table III. Before and after intervention values for functional and physical indices in the studied patients

Variables	Exercise group (n=16)		Control group (n=14)		Levene's test	F	*P*	η	Observed power
	Before	After	Before	After					
BBS	40.37 ± 9.97	46.43 ± 8.34	34.00 ± 9.13	35.85 ± 7.22	0.38	7.01	0.01	0.20	0.72
FRT	10.06 ± 5.80	14.81 ± 5.74	7.28 ± 5.06	7.85 ± 5.50	0.03	2.46	0.12	0.08	0.32
10MWT	17.67 ± 8.92	13.37 ± 4.59	21.16 ± 6.36	19.39 ± 6.52	0.42	0.34	0.56	0.01	0.08
TUG	11.32 ± 5.21	11.16 ± 8.82	14.43 ± 3.20	14.57 ± 4.02	0.61	3.93	0.05	0.12	0.48
Chair rise	32.65 ± 13.52	23.28 ± 4.94	32.63 ± 12.13	33.94 ± 7.27	0.64	1.62	0.21	0.05	0.23
Modified push-up	5.31 ± 4.75	12.12 ± 6.54	2.42 ± 3.99	2.92 ± 3.83	0.04	3.44	0.07	0.11	0.43
6MWT	184.01 ± 101.04	272.32 ± 105.60	150.37 ± 65.18	162.80 ± 60.57	0.32	7.56	0.01	0.21	0.75

BBS, Berg balance scale; FRT, functional reach test; 10MWT, 10-meter walk test; TUG, timed up and go; 6MWT, 6-minute walk test
P, significance; *η*, partial eta-squared (demonstrated the changes of variable); Observed power (to indicate an adequate number of subjects)
Values are mean ± SD

Table IV. Before and after intervention values for Multiple Sclerosis Quality of Life-54 Questionnaire (MSQOL-54) scores in the studied patients

Variables	Exercise group (n=16)		Control group (n=14)		Levene's test	F	*P*	η	Observed power
	Before	After	Before	After					
Physical function	38.43 ± 18.04	48.75 ± 22.09	45 ± 23.36	38.57 ± 18.85	0.05	3.68	0.06	0.12	0.45
Health perceptions	43.75 ± 17.46	52.50 ± 16.02	36.42 ± 14.33	40.35 ± 11.17	0.21	0.00	0.94	0.00	0.05
Energy / fatigue	46.00 ± 9.90	47.75 ± 8.69	42.57 ± 10.71	42.28 ± 8.10	0. 43	0.37	0.54	0.01	0.09
Role limitations - physical	21.87 ± 31.45	26.56 ± 28.09	23.21 ± 30.16	14.28 ± 18.89	0.83	0.03	0.85	0.00	0.05
Pain	55.93 ± 17.01	70.93 ± 17.85	53.09 ± 24.86	62.61 ± 20.08	0.80	0.04	0.83	0.00	0.05
Sexual function	28.64 ± 37.26	24.47 ± 31.62	39.88 ± 36.27	45.23 ± 36.06	0.96	1.58	0.21	0.00	0.07
Social function	65.10 ± 16.72	68.75 ± 15.95	54.76 ± 22.8	61.90 ± 14.51	0.46	0.62	0.43	0.02	0.11
Health distress	51.56 ± 22.33	68.12 ± 22.79	40.71 ± 26.8	53.57 ± 18.23	0.69	0.02	0.86	0.00	0.05
Physical Health Composite	45.80 ± 9.70	53.36 ± 11.9	43.38 ± 15.43	45.53 ± 7.30	0.04	0.40	0.53	0.01	0.09
Health distress	51.56 ± 22.33	68.12 ± 22.79	40.71 ± 26.87	53.57 ± 18.23	0.69	0.02	0.86	0.00	0.05
Overall quality of life	56.35 ± 11.43	58.65 ± 11.13	49.28 ± 18.67	52.26 ± 12.72	0.58	0.12	0.73	0.00	0.06
Emotional well-being	54.25 ± 18.29	61.75 ± 14.74	38.76 ± 21.68	46.76 ± 14.64	0.44	0.49	0.48	0.01	0.10
Role limitations - emotional	29.16 ± 40.13	43.75 ± 39.84	33.33 ± 29.23	40.47 ± 39.61	0.05	0.12	0.72	0.00	0.06
Cognitive function	71.87 ± 22.35	65.62 ± 20.64	58.21 ± 16.71	59.28 ± 16.27	0.03	2.56	0.12	0.08	0.33
Mental Health Composite	50.87 ± 15.46	58.34 ± 14.89	41.66 ± 17.07	50.10 ± 14.72	0.58	0.65	0.42	0.02	0.12
Change in health	40.62 ± 27.19	56.25 ± 26.61	41.07 ± 21.04	42.85 ± 26.72	0.91	1.17	0.28	0.04	0.18
Satisfaction with sexual function	50.00 ± 24.15	54.68 ± 18.75	51.78 ± 11.86	57.14 ± 15.28	0.46	0.00	0.99	0.00	0.05

Physical Health Composite is sum of physical function, health perceptions, energy/fatigue, role limitation-physical, sexual function, social function, and health distress
Mental Health Composite is the sum of health distress, overall quality of life, emotional well-being, role limitation-emotional, and cognitive function
P, significance; η, partial eta-squared (demonstrated the changes of variable); Observed power (to indicate an adequate number of subjects)
Values are mean ± SD

Table V. Before and after intervention levels of hormones in patients

Serum levels	Exercise group (n=16)		Control group (n=14)		Levene's test	η	*P*	F	Observed power
	Before	After	Before	After					
Ghrelin (ng/ml)	6.98 ± 1.31	8.42 ± 0.83	6.24 ± 1.49	7.29 ± 1.71	0.87	1.98	0.17	0.07	0.27
Leptin (ng/ml)	18.02 ± 18.52	15.06 ± 14.48	13.78 ± 7.04	13.67 ± 5.60	0.57	0.91	0.34	0.03	0.15
Ghrelin/Leptin	1.12 ± 1.16	2.59 ± 3.28	0.64 ± .46	0.64 ± 0.40	0.75	0.26	0.61	0.01	0.07
Testosterone (ng/ml)	2.21 ± 3.05	2.56 ± 3.97	1.43 ± 3.43	1.21 ± 2.81	0.84	0.59	0.44	0.02	0.11
Testosterone/Leptin	0.77 ± 1.36	1.91 ± 3.76	0.23 ± 0.69	0.15 ± 0.42	0.62	0.00	0.98	0.00	0.05

P, significance; *η*, partial eta-squared; (demonstrated the changes of variable); Observed power (to indicate an adequate number of subjects)
Values are mean ± SD

Our study showed significantly increased balance after training sessions. In our earlier study[25], after eight weeks of WBV training on MS patients the training group showed a significant increase in balance. Claerbout *et al*[15] demonstrated after three weeks WBV in hospitalized MS persons, the Berg balance score was larger in training group than in the control group, but not significant. Another study showed that the WBV had significant improvements in standing balance from baseline[16]. Previously, Schuhfried *et al*[6] studied the effect of whole body vibration at low amplitude (2.0-4.4 HZ oscillations at 3-mm amplitude) on 12 MS patients with moderate disability (EDSS 2.5-5), and they showed that WBV training had a positive influence on mobility and postural control. Balance problems are caused by a limited capacity to integrate visual, proprioceptive and vestibular stimuli for determination of the position of the body in space[5]. Mason *et al*[16] showed that the WBV caused significant improvements in the time of 10-m walk at eight weeks. Another study[21] reported four weeks vibration therapy in multiple sclerosis causing non significant improvement in 10-m walk. The result of our study showed no significant effect on walking speed and endurance similar to other studies[16,17,21]. Our study showed no significant effect on functional mobility (chair rise time). In a study three-week WBV training showed no significant effect on chair raise test[17]. Our study demonstrated no significant effect in muscle endurance but significantly increase in walking endurance (6MWT). Hilgers *et al*[17] reported that three weeks of WBV caused significantly greater improvements in the 6-min walk test in MS patients. In addition, the walking distance (6MWT) was found to be inversely related to the EDSS scores[1,26]. Previous studies have shown that WBV is associated with an increase in lower limb muscle strength, which is essential for postural stability[21,26]. Schyns *et al*[21] studied the effects of WBV training in 16 MS patients, and observed that WBV could have positive effects on muscular force and muscle spasm of MS patients. Delecluse *et al*[26] have suggested that WBV has a great potential in a therapeutic context where it may enhance muscular performance in patients and elderly, who are not able to perform standard exercise programme. WBV provides a strong sensory stimulus which activates the muscle spindles, which might enhance proprioception, which in turn might be the reason for improvement in balance with WBV training[5]. It seems that this increase in distance during six minutes walking in MS patients, obtained following WBV training may be due to the effects of the training on the recruitment of more motor units[1].

Previous studies on WBV training in MS had not focused on the role of functional, physical, psychosocial, and hormonal changes in MS patients. Also, the results showed that WBV training had no significant changes in leptin, ghrelin, ghrelin/leptin ratio, testosterone, and testosterone/leptin ratio. Leptin, a cytokine-like hormone with T helper 1 (Th1) promoting effects, may play a pathogenic role in MS and can be a useful marker of disease activity and response to therapy[9,26,27]. It has also been shown that ghrelin mediates opposite effects of leptin on peripheral immune responses. In fact, ghrelin blocks the leptin-induced secretion of proinflammatory cytokines[9]. Increase in levels of ghrelin due to improvement in physical fitness could also be responsible for the observed improvement in MS patients, which might be due to anti-inflammatory effects of ghrelin[28].

Sicotte *et al*[29] have suggested that testosterone treatment has potential neuroprotective effects in men with relapsing-remitting MS. Another study showed a significant increase in testosterone hormone concentration and neuromuscular performance following WBV in healthy men[10] and suggested that WBV influenced proprioceptive feedback mechanisms and specific neural components, leading to improvement of neuromuscular performance[4,6]. In an earlier study no significant changes were identified in salivary concentration of testosterone in responses to a single session of whole body vibration exercise in healthy young men[30].

In conclusion, our results showed that long term use of WBV might create positive effects on EDSS and some variables of physical fitness in MS patients, but no improvement in quality of life and fatigue. In addition, WBV showed no change in the serum levels of ghrelin, leptin, ghrelin/leptin ratio, testosterone, and testosterone/leptin ratio. These positive effects of WBV could be temporary, and related to the duration of the protocol and detraining could lead to a reduction or loss in the effects of WBV. However, the effects of this method of training can be valuable as effective factors in reducing patient's inability.

***Conflicts of Interest*:** None.

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