RESPIRATORY TRAINING IMPROVES RESPIRATORY MUSCLE FUNCTION, EXERCISE CAPACITY AND FATIGUE IN PATIENTS WITH MS: A RANDOMİZED CONTROLLED TRIAL

MS'Lİ HASTALARDA SOLUNUM EĞİTİMİ SOLUNUM KASLARI FONKSİYONLARINI, EGZERSİZ KAPASİTESİNİ VE YORGUNLUĞU DÜZELTİR: RANDOMİZE KONTROLLÜ BİR ÇALIŞMA

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SUMMARY

Objectives: Respiratory involvement may occur early in the course of MS disease. The purpose of this study was; to evaluate the effects of respiratory training program on respiratory muscle function, exercise capacity and fatigue in MS patients.

Materials and methods: Twenty patients with MS participated in a conventional MS rehabilitation program. For the same period, the respiratory training group received an additional 30 minutes of respiratory muscle training for 6 week.

Results: After the training program, there was a statistically significant increase in PI max and PE max in the training group compared to the baseline (p= 0,010 for PI max, p= 0,011 PE max) and there was a statistically significant increase in PI max and PE max in the training group compared to the control group (p= 0,016 for PI max, p= 0,021 for PE max). This was also associated with improvements in exercise capacity, and fatique.

Conclusions: Significant short-term effects of the respiratory muscle training program on respiratory muscle function, exercise capacity and fatigue were recorded in this study. We suggest that MS patients should receive respiratory muscle training to avoid respiratory problems and deconditioning.

Key words: MS, respiratory training

ÖZET

Amaç: Solunum sistemi tutulumu MS hastalığı sürecinde erken dönemde oluşabilir. Bu çalışmanın amacı; MS'li hastalarda solunum eğitiminin solunum kasları fonksiyonları, egzersiz kapasitesi ve yorgunluk üzerindeki etkilerini değerlendirmektir.

Materyal ve metod: MS'li 20 hasta konvansiyonel MS rehabilitasyon programına katıldılar. Aynı dönemde solunum eğitimi grubu, ilave olarak 6 hafta boyunca otuz dakikalık solunum kası eğitimi aldılar.

Bulgular: Eğitim programı sonrasında, giriş değerleriyle (p= 0,010 for PI max , p= 0,011 PE max) ve kontrol grubuyla (p= 0,016 for PI max, p= 0,021 for PE max) karşılaştırıldığında PI max ve PEmax eğitim grubunda istatistiksel olarak anlamlı şekilde arttı. Bu egzersiz kapasitesi ve yorgunlukta düzelme ile birlikteydi.

Sonuç: Bu çalışmada solunum kasları eğitim programının solunum kasları fonksiyonları, egzersiz kapasitesi ve yorgunluk üzerinde kısa süreli anlamlı etkisi saptandı. MS hastalarının solunum problemleri ve kondüsyon bozukluğunun önlenmesi için solunum kasları eğitimi almasını öneriyoruz.

Anahtar kelimeler: MS, solunum eğitimi

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INTRODUCTION

Respiratory complications are major causes of morbidity and mortality in patients with MS. Atelectasis, aspiration and pneumonia has long been recognized for advanced MS patients (1-5).

Patients with MS also show a poor exercise tolerance and reduced physical, recreational and social activities (6-9). Neurological deficits promoting a sedentary life style may lead to declining cardiovascular fitness, disuse atrophy and weakness in MS patients. Little attention is generally paid to the pulmonary system during the examination of MS patients, probably because of these patients are free from pulmonary symptoms or disease. However, respiratory involvement may occur early in the course of this disease (1,2,5).

Based on these findings, respiratory muscle training programs have been hypothesized for MS patients to enhance exercise tolerance and to improve respiratory dysfunction (10). The purpose of this study was; to evaluate the effects of breathing retraining, ventilatory and upper extremity muscles training program on respiratory muscle function, exercise capacity and fatique in MS patients.

MATERIAL AND METHODS

Subjects

Twenty patients with definite MS (10M, 10F) were recruited from inpatient rehabilitation department of the Ankara Physical Medicine and Rehabilitation Education and Research Hospital. Before participating in the study, subjects underwent a complete medical assessment that included medical history, physical and neurological examination, posteroanterior teleradiograph, a resting 12 lead electrocardiogram (ECG) and routine laboratory measurements. The criteria for recruitment of subjects for the study were: 1) sufficient upper torso and extremity nerve function and strength to accomplish arm crank ergometry (ACE), (2) ability to understand and follow simple verbal instructions, 3) no previous history of cardiovascular or respiratory problems, 4) no medication that would influence metabolic or cardiorespiratory responses to exercise, and 5) no previous history of regular exercise training and sports activity to strengthen upper extremity and ventilatory muscles.

The exclusion criteria included chronic pulmonary and/or cardiac disease, clinical signs of cardiac and/or respiratory disease, impaired level of consciousness and evidence of gross cognitive impairment.

The hospital's ethical committee approved the study, and all patients gave informed consent.

Study Design

All subjects underwent a standardized interview regarding their current medications, physical activity level and smoking habits. Body weight was measured with subjects wearing light clothing. Since some subjects were unable to stand, arm span was used to obtain height. Body mass index was calculated as the ratio of body weight and height squared (kg/m2). We used a randomized controlled design in which the assessor was blind to the group allocation of the subject. Blinding the patients was not possible due to the nature of the treatment. An independent physician who did not otherwise participate in the study took charge of the randomization process. After informed consent and baseline data collection, stratified, variable block randomization was used to assign eligible participants to 1 of the 2 groups. The factor used for stratification was gender. The randomization assignment was generated by random numbers obtained from a statistics textbook.

Training program

Training was performed at the cardio-respiratory rehabilitation unit of the hospital. Each session in exercise training group consisted of 15 min of diaphragmatic breathing (DB) combined with pursed-lips breathing (PLB), 5 min of air-shifting techniques (A-ST) ,10 min of voluntary isocapneic hyperpnea (VIH) and followed by arm crank exercise. Arm crank exercise program was started with 75 % of the maximum VO2 achieved during a baseline CPET. Exercise intensity was gradually increased to maximal exercise as tolerated. The patients had a 5- min interval before each type of exercise. The training was performed three times for over 6 weeks.

Both the training group and nontraining group also participated in a conventional MS rehabilitation program, 5 days a week for 6 week. Conventional rehabilitation program included range of motion and strengthening exercises for upper and lower extremities, neurophysiologic techniques, balance and coordination training, ambulation training, control of spasticity and management of bladder and bowel dysfunction and communication disorders.

Outcome Measures

Outcome measures were repeated at baseline (pre-treatment) and at end of training programme 6 week (post-treatment). A same physiatrist, blinded to the type of training programme, evaluated changes with training programme.

Pulmonary function, resting spirometric measurements including forced vital capacity (FVC), vital capacity (VC), forced expiratory volume at one second (FEV1), the ratio of FEV1 to FVC (FEV1/FVC), forced expiratory flow rate 25-75% (FEF 25-75%), peak expiratory flow rate (PEF) and maximum voluntary

Tablo I

The subjects characteristics of the training and nontraining group.

	Training	Nontraining	p values
	Mean ± SD	*Mean ± SD*	
Age (y)	37,33 ± 8,06	39,00±8,28	p>0,05
Body mass index (kg/m^2)	24,11± 5,35	24,20±3,65	p>0,05
Disease duration (m)	72,33 ± 59,00	46,62± 58,28	p>0,05
EDSS	4,39 ± 2,32	4,5 ± 2,61	p>0,05
Gender			p>0,05
Female	6/10	6/10	
Male	4/10	4/10	
Ambulation status			
Ambulatory	4/10	4/10	
Required assistance	4/10	3/10	
Nonambulatory	2/10	3/10	
Smoking habit			
Lifetime nonsmoker	6/10	6/10	
Ex-smoker	2/10	1/10	
Current smoker	2/10	3/10	

(F: Female, M: Male, EDSS: Expanded Disability Status Scale, SD: Standard deviation)

ventilation (MVV) were performed on a hand-held spirometer (Sensormedix, Vmax29, Yorba Linda, CA, USA). All studies were performed in a sitting position. Each subject performed at least three trials and the best performance was used for analysis. Measurements were expressed as percentages of the predicted values. Eighty percent of predicted maximum or greater was accepted as normal. The maximum inspiratory and expiratory pressures (PI max, PE max) were obtained using a digital mouth pressuremeter (MPM, Sensormedix, Yorba Linda, CA, USA). The PI max measured following exhalation to residual volume (RV) and the PE max, following inspiration to total lung capacity. Each measure was repeated three times. The subject's best sustained effort for one second was used for data analysis. Values greater than 70-90 cmH2O for PI max and 80-100 cmH2O for PE max were taken as normal.

Cardiopulmonary exercise test (CPET), was performed on an electronically braked arm crank ergometer (Sensormedix, Ergoline, Yorba Linda, CA, USA). A computerized gas analysis system collected and analysed expired gases during exercise (Sensormedix Vmax29, Yorba Linda, CA, USA). A standard open-circuit method was used to collect expired gases. It was calibrated with known gas concentrations and volumes prior to each test. Heart rate and ECG were displayed throughout the CPET test. Capillary oxygen tension was measured by an oxygen photometer attached to the ear lobe. An incremental exercise test was used to determine maximum exercise performance. After stabilization and a 3-minute warm-up period at 25W, the load was increased every 3 minutes until exhaustion. The subjects were instructed to maintain a crank rate of 50 RPM and verbally encouraged to continue exercise as long as possible. Oxygen consumption (VO2), carbon dioxide exhaled (VCO2), minute ventilation (VE), respiratory rate (RR), respiratory exchange ratio (RER), the ratio of physiologic dead space to tidal volume (VD/VT), oxygen saturation (SaO2), and power output (PO) were recorded every 2 seconds during the CPET. Anaerobic threshold was determined by computerised V-slope method of the gas exchange data.

Fatigue severity scale (FSS) was used to measure the impact of excessive fatigue on daily function. The scale consists of nine statements related to fatigue (11).

The Kurtzke Expanded Disability Status Scale (EDSS) were used to describe levels of neurological functioning (12).

Data analysis

All data were entered into a database for later analysis (SPSS, version 11,0 for Windows, SPSS Inc, Chicago, IL). Chi square analysis was calculated to examine differences in frequencies for categorical variables. Demographic and clinical data were compared between the groups with independent-sample t test analysis. Pearson's correlation coefficients were used to examine the relationship between continuous variables. Spearman correlation coefficients were used to examine the relationship between categorical variables.

Results

The clinical and demographic features of the patients are shown in table 1. There was no differences between the groups as regards age, height, weight, body mass index, duration of the disease and EDSS at the beginning of the study.

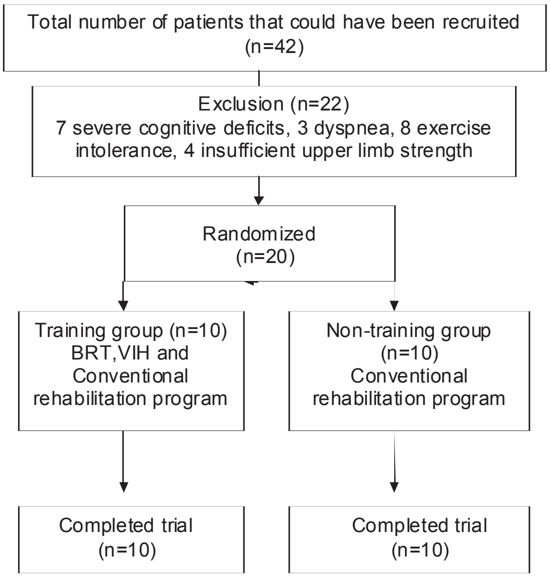

Figure 1. Flow diagram of participants to the trial

Pulmonary Function

Table 2 shows the mean resting spirometric values and respiratory muscle function in MS subjects at baseline and at the end of the sixth week.

No significant difference was determined as regards FVC, VC, FEV1, FEF 25-75%,MVV and PEF in the training group at the end of the training compared to baseline and compared to the nontraining group .

Inspiratoy Muscle Strength

In comparison with the normal values, we observed a substantial decrease in baseline PI max and PE max measures of all groups .

After 6 week of training, there was a statistically significant increase in PImax and PE max in the training group compared to the baseline and the nontraining group.

Exercise Capacity

When compared to the baseline values and the control group, statistically significant improvement was

Tablo II

Pretraining and posttraining resting spirometric values and respiratory muscle function of the MS patients.

Variables	n	Pre-training	Post-training	p value*	*p value***
FVC					
Training group	10	4,064 ± 0,49	4,071±1,00	0,397	0,252
Nontraining group	10	3,39±1,70	3,4±1,6	0,600	
FEV1					
Training group	10	3,46±0,83	3,50 ±0,90	0,735	0,314
Nontraining group	10	2,71±1,30	2,7±1,3	1,000	
VC					
Training group	10	4,067± 0,95	4,08 ±0,97	0,612	0,774
Nontraining group	10	3,46±1,61	3,4±1,5	0,462	
PEF					
Training group	10	6,31±1,87	6,23±1,53	0,398	0,830
Nontraining group	10	4,98±1,68	4,7±1,8	0,345	
$FEF_{25\text{-}75\%}$					
Training group	10	95,62±13,10	99,57±18,77	0,395	0,317
Nontraining group	10	74,3±25,5	71,8±34,5	0,345	
MVV					
Training group	10	105,37±26,94	102,57±36,43	0,933	0,352
Nontraining group	10	85,8±39,3	77,6±37,2	0,580	
PI max					
Training group	10	36,62±12,58	39,50±13,25	0,010*	0,016**
Nontraining group	10	36,6±9,5	37,8±9,4	0,034	
PE max					
Training group	10	68,62±10,52	71,75±13,43	0,011*	0,021**
Nontraining group	10	55,6±18,4	54,5±16,3	0,285	

The values were expressed as mean±standard deviation. FEV_1 : forced expiratory volume in one second, FVC: forced vital capacity, VC: vital capacity, FEF%25-75: forced expiratory flow rate 25-75%, PEF: peak expiratory flow rate, MVV: maximum voluntary ventilation, PImax:maximum inspiratory pressure,PEmax: maximum expiratory pressure
* Training group had significantly PImax and PEmax values compared to baseline.
** Training group had significantly PImax and PEmax values compared to nontraining group.

Tablo III

Pretraining and posttraining Exercise capacity and FSS values of the MS patients.

Variables	n	Pre-training	Post-training	P value*	P value**
VO2 peak (ml/kg/min)					
Training group	10	9,62± 3,75	12.48±0.83	0.001*	0.010 **
Nontraining group	10	8,9±3,90	10,30±3,99	0,463	
PO (watt)					
Training group	10	37,12± 4,29	37,28±5,02	0,914	0,514
Nontraining group	10	32,8±8,10	31±14,08	0,500	
Exercise time					
Training group	10	12,06± 2,56	14,78± 5,67	0,161	0,196
Nontraining group	10	13,6±4,90	14,8±2,40	0,225	
FSS					
Training group	10	5,75±2,13	5,36±1,21	0,010*	0,009**
Nontraining group	10	4,9±1,30	5,05±1,63	0,173	

The values were expressed as mean±standard deviation. VO_{2peak}: peak oxygen consumption; PO: power output; FSS:fatique severity scale
*Training group had significantly $VO_{2peak\ and}$ FSS values compared to baseline.
** Training group had significantly $VO_{2peak\ and}$ FSS values compared to nontraining group.

observed in the values of VO2, but not in the PO and exercise time at the end of the training (table 3).

FSS

The improvement in fatigue severity scale was statistically high in the training group compared to the baseline and the control group.

Discussion

This study demonstrated that respiratory muscle and arm cranck exercise training program improve respiratory muscles function in MS patients. This was associated with improvements in exercise capacity and fatique severity.

Previous studies reported that respiratory muscles and aerobic exercise training improved respiratory muscles weakness and exercise capacity in MS population (13-16). These improvements maintained 1-6 months after the training period ended. Inspiratory resistive loading or inspiratory threshold loading devices were used to train respiratory muscles in these previous studies.

Pursed-lips breathing, air-shifting and diaphragmatic breathing are breathing retraining techniques. The goals of breathing retraining are to restore the diaphragm to a more normal position and function, to decrease the respiratory rate, to diminish the work of breathing, to reduce dyspnea, to improve chest wall motion, ventilation distribution and expiration by preventing airway compression and airway collapse and to increase exercise performance (17,18).

The methods of respiratory muscle training are voluntary isocapneic hyperpnea, inspiratory resistive loading and inspiratory threshold loading. Voluntary isocapneic hyperpnea provides low tension and a high level of repetitive activity for the diaphragm and other inspiratory muscles. VIH have been shown to improve the strength and endurance of respiratory muscles (19).

In our study, BRT and VIH techniques were used to train respiratory muscles. We think BRT and VIH are easy ways to train respiratory muscles, since this type of exercises is not required equipment.

The major function of expiratory muscles is to generate a forceful and effective cough. Expiratory muscle weakness causes ineffective cough, retention of secretions, and inability to maintain a clear airway. These conditions may lead to pneumonia and atelectasis. Several studies have indicated that approximately half of the patients died from complications of MS, with pneumonia being the most frequent underlying cause (1,4,5). In our study, exercise training program has been shown to improve expiratory muscle strength in MS patients. Improved expiratory muscle strength may decrease retention of secretions and the risk of respiratory infections in these populations.

Pulmonary rehabilitation has no effect on the principal physiological abnormalities in pulmonary disease. Therefore, spirometric values are not changed after the rehabilitation program (19). As in previous report, spirometric values of our patients did not differ after the training program.

The measurement of peak oxygen uptake (VO2max) is considered to be the best measure of cardiorespiratory fitness and exercise capacity. Peak power output (PO) is a second important indicator of exercise capacity (20). Patients with MS show a poor exercise tolerance and reduced physical, recreational and social activities (6-9). Our results supported that exercise capacity and fatique severity have been improved by respiratory muscles and upper extremity training program in patients with MS.

The main limitation of our study is that longterm effects of respiratory muscles training were not provided in our patients. There is consensus that exercise programs shorter than 6 to 8 weeks are less effective (17,18). Our patients have been trained during for six weeks that is considered as an effective time. We also recommended our patients that they perform their exercises regularly at home. However, It has been proved in a previous study that compliance with maintenance home exercise therapy is relatively low (18). Therefore, we suggest to determine the long term effect of increasing respiratory muscles strength in MS populations. Another limitation of this study is that the number of patients, who are in volved in this study,was substantially low.Some useful effects recorded on clinical and laboratory parameters are promises us. Yet, these findings are insufficient for concluding that respiratory training can favorably improve respiratory muscle function, exercise capacity and fatique. Controlled studies in a larger group of patients are needed to determine the effects of respiratory training in MS.

Respiratory muscles function, and especially inspiratory muscle function , has been shown to contribute dyspnea, exercise limitation, deconditioning, hypercapnia and reduced quality of life in patients with COPD (17). These important observations suggested that respiratory muscles training might be able to improve exercise performance, symptoms and quality of life in COPD patients. In fact, previous studies showed that respiratory muscles training was associated with significant improvements in respiratory muscles strength and endurance, exercise capacity, power output and dyspnea (17,21).

Consistent with previous studies in COPD, we observed that respiratory muscles training plays an important role in respiratory muscles strength, exercise capacity and fatique severity in MS subjects .

The presence of problems such as mobility limitations, sensory-perceptual dysfunctions and communication deficits has discouraged the systematic application of cardio-pulmonary exercise testing (CPET) to determine respiratory function in MS population. Therefore, unless patients have evident pulmonary semptom or disease , traditional MS rehabilitation programs generally includes therapeutic approaches to the motor control (upper limb and walking); spasticity; cognition, language and communication disorders; swallowing and nutrition; fatique; bowel and bladder control and psychosocial problems (22)

Since respiratory muscles strength plays a strong role in exercise capacity and in most of the cardiopulmonary responses to exercise, systematic measurement of respiratory muscles function should be considered in MS populations. Once respiratory muscles impairment and respiratory dysfunction is determined ,respiratory muscle training should be carried out.

Significant short-term effects of the respiratory muscles training program on respiratory muscles function, fatique and exercise capacity were recorded in this study. Our findings suggest that respiratory muscles and upper extremity training should be considered to avoid respiratory problems, deconditioning and fatigue in patients with MS. Further research is necessary to determine the long term effect of increasing respiratory muscles strength on clinical outcomes in those populations.

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