Doi: 10.4274/npa.y6091

Quality of Life, Fatigue and Balance Improvements after Home-Based Exercise Program in Multiple Sclerosis Patients

Multipl Skleroz Hastalarında Ev Egzersiz Programının Sonrasında Yaşam Kalitesi, Yorgunluk ve Dengedeki İyileşmeler

Özge ERTEKİN, Serkan ÖZAKBAŞ*, Egemen İDİMAN*, Z.CANDAN ALGUN**

Dokuz Eylül University School of Physical Therapy and Rehabilitation, Izmir, Turkey

ABSTRACT

Objectives: To determine the effects of home-based exercise program (HEP) on aspects of disability, quality of life (QoL), fatigue and balance in multiple sclerosis (MS) patients.

Method: 40 MS patients were enrolled in the study. Demographic, socioeconomic and medical statuses were recorded. Disability [Expanded Disability Status Scale (EDSS)], functional balance [Berg Balance Scale (BBS)], perceived level of balance confidence in everyday tasks [Activities-specific Balance Confidence (ABC) Scale)], fatigue [Fatigue Impact Scale (FIS)], and QoL [Multiple Sclerosis International Quality of Life (MusiQoL) questionnaire] were assessed at baseline and 3 months later. All participants received standardized 12-weeks HEP from an experienced physiotherapist.

Results: There were no statistically significant differences in EDSS scores before and after treatment (p=0.41). All patients showed significant improvement in BBS, ABC scale, and MusiQoL scores (p<0.001), and in the cognitive, physical and social components of FIS from baseline to three months (p=0.002, p=0.001, p=0.002, respectively). A statistically significant difference was not found in FIS-total scores (p=0.060). A positive significant correlation was found between MusiQoL and FIS-total scores (p<0.001), cognitive (p=0.004), physical and social (p<0.001) subscores; as well as negative correlation between QoL and ABC scale scores (p<0.001).

Discussion: Home-based exercise program resulted in improvements in QoL, fatigue and balance functions in MS individuals. Therefore, neurological rehabilitation professionals, who are specialized on this area, have to consider the benefits of exercise and physical activity for MS patients and encourage them to take part in an exercise program. (*Archives of Neuropsychiatry* 2012;49: 33-8) **Key words:** Multiple sclerosis, home exercises, quality of life, fatigue, balance

ÖZET

Am aç: Bu çalışmanın amaçları, Multipl Skleroz (MS) hastalarında ev temelli egzersiz eğitiminin yetiyitimi, yaşam kalitesi, yorgunluk ve denge üzerine etkilerini saptamaktır.

Yöntemler: Kırk MS hastası çalışmaya dahil edilmiştir. Hastaların, demografik, sosyoekonomik ve medikal düzeyleri kaydedilmiştir. Yetiyitimi [Expanded Disability Status Scale (EDSS)], fonksiyonel denge [Berg Denge Skalası (BDS)], günlük aktivitelerde algılanan güven duygusı [Aktiviteye Spesifik Denge Güvenlik Skalası-ABC], yorgunluk [Yorgunluk Etki Skalası (YES)] ve yaşam kalitesi [Multiple Sclerosis International Quality of Life (MusiQoL) questionnaire] değerlendirmeleri tedavi öncesinde ve 3 ay sonra tekrarlandı. Tüm katılımcılara, fizyoterapist tarafından 12 haftalık standardize ev-temelli egzersiz programı verildi.

Bulgular: Hastaların tedavi öncesi ve sonrasında EDSS skorları arasında istatistiksel olarak anlamlı fark yoktu (p=0,41). Tüm katılımcılar, egzersiz programından sonra BDS, ABC ve MusiQoL skorlarında (p<0,001), YES'nın kognitif, fiziksel ve sosyal komponentlerinde iyileşme kaydetti (sırasıyla, p=0,002, p=0,001, p=0,002). YES-total skorlarında ise istatistiksel olarak anlamlı fark yoktu (p=0,060). MusiQoL ile YES-total (p<0.001), MusiQoL ile YES-kognitif (p=0,004), YES-fiziksel (p<0,001), YES-sosyal altgrupları arasında (p<0,001) istatistiksel olarak anlamlı pozitif korelasyon; MusiQoL ile ABC arasında ise istatistiksel olarak anlamlı negatif korelasyon saptandı (p<0,001).

Sonuç: MS hastalarında, ev-temelli egzersiz programı, yaşam kalitesi, yorgunluk ve denge fonksiyonlarında iyileşmeyle sonuçlanmıştır. Bu nedenle bu alanda çalışan nörolojik rehabilitasyon ekibinin, MS hastalarında fiziksel aktivite düzeyini artırmaya odaklanmasının ve hastaları egzersiz yapmaları için cesaretlendirilmesinin önem taşıdığını düşünmekteyiz. (Nöropsikiyatri Arşivi 2012;49: 33-8)

Anahtar kelim eler: Multipl skleroz, ev egzersizleri, yaşam kalitesi, yorgunluk, denge

Introduction

Multiple sclerosis (MS) is a chronic demyelinating disease resulting in functional limitations, disability and reduced quality of

life (QoL) through the impairments such as muscular weakness, ataxia, spasticity, balance dysfunction, general fatigue, sensory disturbances, and visual vestibular disturbances (1). Within 15 years after MS diagnosis, 50% of patients will have walking

^{*}Dokuz Eylül University School of Medicine, Department of Neurology, İzmir, Turkey

^{**}Istanbul Medipol University Faculty of Medical Science Department of Physiotherapy and Rehabilitation, Istanbul, Turkey

impairment and 10% will be restricted to a wheelchair (2). Additionally, MS patients have reduced physical functioning and decreased levels of physical activity (3), which may lead to physical deconditioning and increased risk for secondary conditions such as coronary heart disease (4,5). Inactivity and functional disability may be held responsible for social isolation in individuals with MS (4). Cross-sectional studies suggested regular physical activity for the solution of problems associated with inactivity and for improvements in QoL (6-8). However, the advantages of different types of exercise programs are not clearly documented (9-13). This study was designed to determine the effects of home-based exercise training on aspects of disability, quality of life, fatigue and balance in different disability levels of MS.

Method

A total of 40 patients with MS, referred for rehabilitation to the Multiple Sclerosis Outpatient Clinic of Neurology Department at Dokuz Eylul University School of Medicine between October 2008 and July 2009, were evaluated.

Patients were admitted into the study if they satisfied the following criteria: 1) diagnosis of clinically or laboratory definite relapsing remitting, primary progressive or secondary progressive MS according to Poser's criteria (14), 2) ability to stand independently, 3) age between 18 and 65 years, 4) EDSS≤6.5, 5) cooperation, and 6) volunteer to join to the study.

Patients were excluded if their diagnosis was not clearly established; they were suffering from an acute relapse (within the last 30 days) prior to the first examination; they had history of cardiovascular, respiratory, orthopedic, psychiatric, or other medical comorbidities, and they were participating a regular physical activity within the last six months. Regular physical activity assessment was made according to patients' self-record if they have attended to a regular activity within the last six months such as taking a regular exercise program, having regular sport/leisure time activities.

40 MS patients met the inclusion criteria and were enrolled in the study. Written informed consent was received from all participants. Patients were regarded as drop-outs if they had a relapse or new concurrent illness during the study period. A physical therapist administered the evaluation scales which consisted of the Berg Balance Scale (BBS), Fatigue Impact Scale (FIS), Activites-specific Balance Confidence (ABC) Scale and Multiple Sclerosis International Quality of Life (MusiQoL) questionnaire. Expanded Disability Status Scale (EDSS) was performed by a neurologist. All patients were instructed to continue exercising for 12 weeks at home. The patients were provided with an individual exercise program instructed by a physiotherapist based on a standardized rehabilitation program. The subjects kept a daily diary in which they recorded their adherence and progress for individual feedback and encouragement.

Assessment

Demographic characteristics and medical history were recorded by a questionnaire included information on age, gender, height, weight, and body mass index, marital status, education, employment, assistive device use, disease duration, and EDSS score.

Measurement of Disability

The severity of disability was determined based on the EDSS scores as mild disability (EDSS \leq 3.5), and severe disability (EDSS 4.0-6.5) (15,16).

Measurement of the Perceived Impact of Fatigue

Perceived impact of fatigue on daily activities was investigated with the Turkish version of the Fatigue Impact Scale (17). This scale is a multidimensional scale that comprises 40 items measuring physical (%), cognitive (%) and social (%) effects of fatigue. Each item assessed fatigue during the past 30 days. Rating was made on a four-level scale from 0 (no problem) to 4 (extreme problem). The total score (%) was calculated by dividing the sum of the three three sub-scores which gives the degree of impact of fatigue (17,18).

Measurement of Functional Balance

Balance was assessed using the Berg Balance Scale, a task performance test consisting of 14 items of increasing difficulty graded on a five-point ordinal scale from 0 to 4 [0= unable to perform task, 4= independent] (19). Higher scores reflect a better level of balance ability. An overall score of less than 45 points, out of a maximum of 56, is associated with a 2.7- times increase in the risk of a future fall. The reliability of the BBS has been established with a sample of subjects with MS (20).

Measurement of Balance Confidence

The perceived level of confidence while performing everyday tasks was assessed with the ABC Scale (21). The reliability and validity of this scale are found to be good for MS (22,23).

Measurement of the Quality of Life

Multiple Sclerosis International Quality of Life (MusiQoL) questionnaire is a multi-dimensional, self-administered questionnaire, disease-specific quality of life scale. Lower scores show higher level of quality of life. Significant correlations were found between activity in daily life scores and clinical indices. The validity and reliability of the MusiQoL were established in patients with MS (24).

Intervention

All the participants were given basic instructions related to the exercise program. The difficulty of the exercise program based on set criteria by increasing the number of repetitions (from 2 sets of 10 to 3 sets of 15) and by reducing arm support was dependent on an individual's ability. Intensity of training was, during weeks 1-5, one set of 10-12 repetitions; in the sixth week, two sets of 10-12 repetitions and, in the week 12, the number of repetitions was increased to 12-15. All patients were given a written exercise program and were encouraged to exercise with weekly calling by the physical therapist through the intervention. Each participant performed 5 to 10 minutes of warm-up activities such as walking and stretching, 20 to 25 minutes of strengthening and balance exercises, and 5 to 10 minutes of a cool-down period devoted to flexibility and range of motion exercises performed in a seated position (10-15 min), 5 times a week. Training period exercises involved the following: 1) weight bearing activities [chair pushupsl. 2) standing up from a chair and sit-to-stand movements. 3) walking forward and sideways over obstacles, 4) stepping forward and sideways on the exercise stepper, 5) partial squats, 6) calf rises with/without support, 7) tandem stepping and walking with/without support, 8) standing balance and one-foot stance, 9) walking in different direction, 10) upper extremity exercises without/with weights (7,8,10,25).

Data Management and Statistical Methods

All statistical analyses were performed using SPSS the Statistical Package for the Social Sciences Software (version 15.0). All results are reported as mean and standard deviations (SD). Descriptive statistics were used to summarize demographic and baseline characteristics. Potential baseline differences for Fatigue Impact Scale, MusiQoL questionnaire, Berg Balance Scale, and ABC scale scores of the patients were analyzed using Student's-t test. All analyses were performed on an intention-to-treat basis. Means and standard deviations were calculated for each clinical test. The level of significance was set at p<0.05.

Pearson's correlation coefficients were calculated to assess the associations between the scores of QoL, FIS, BBS, ABCS and EDSS. A correlation of <0.3 was considered weak, between 0.3 and 0.7 as moderate, and \geq 0.7 as strong (26).

Results

During the study, nine participants were unable to complete the study because of an MS exacerbation. Therefore, 31 patients - 16 female and 15 male - were included in the final analysis.

Baseline demographic and clinical features of the patients are displayed in Table 1. The mean age of the participants was 43.6 (SD 8.2) years. The disease duration, defined as time since definite diagnosis of MS, was mostly 1-10 years (68%). The sample consisted mostly of married (87%), employed (32%) and educated (52% had >11 years of education and 48% had 5-11 years of education) subjects (Table 1). The adherence to the home-based

Age (y)	43.6±8.2		
Gender (F/M)	16/15		
Weight (kg)	71.1±12.4		
Height (m)	1.7±0.1		
Body Mass Index (kg/m²)	25.1±3.8		
Marital Status			
Married	27		
Single	4		
Education			
5- 11 years	15		
>11 years	16		
Employment			
Retired	15		
Employed	10		
Other	6		
Assistive Device use			
Canadian	16		
None	15		
Disease Duration			
1-10 years	21		
>10 years	10		
EDSS group			
Low disability (≤3.5)	13		
High disability (4.0-6.5)	18		

exercise program that was recorded with a daily diary was successful. The participants completed 90.8% of the 60 exercise sessions (mean 54.5, SD 3.4).

Table 2 shows the outcome measures at baseline and 12th week. The baseline mean±SD score of the EDSS was 4.62±1.29 (range: 2.0-6.0); and posttreatment EDSS score was 4.54±1.39 (range: 2.0-6.5). There were no statistically significant differences in the EDSS scores before and after treatment (p=0.41). According to the BBS, the baseline mean±SD score of the patients was 42.9±7.1 (range: 23-51). After the 12-week training, patients showed significant improvement in balance functions with the mean±SD score of 47.3±5.2 (range 34-54) (p<0.001). In all patients, ABC scale scores tended to improve from baseline (44.1±19.9, range:12-79) to three months (52.9±19.3, range: 14-83) (p<0.001).

Assessed with FIS, the total fatigue level of the participants was 42.7±15.7 at baseline (range: 13-81) and 37.2±18.2, posttreatment (range: 9-83). There were no statistically significant differences in the FIS-total scores before and after treatment (p=0.060). The baseline scores of the subgroups of FIS were found for cognitive component: 37.9±16.5 (range: 8-75), for physical component: 48.2±20.7 (range: 8-85), and for social component: 42.5±15.3 (range: 11-85). At the posttreatment assessment, these mean scores were 31.5±18.3 (range: 6-80); 37.6±20.3 (range: 3-83); 35.9±17.4 (range: 5-84), respectively. It was observed that all participants showed significant improvement in levels of fatigue on the cognitive, physical and social components of FIS during 12-week home exercise (p=0.002, p=0.001, p=0.002, respectively).

The mean baseline MusiQoL score was 42.4 ± 14.2 (range: 13.7-69.2), and posttreatment score was 34.7 ± 14.1 (range: 12.9-64.5). There was significant difference between baseline and posttreatment MusiQoL scores of patients (p<0.001) (Table 2).

A positive significant correlation was found between MusiQoL score and FIS total score (r = 0.589, p < 0.001), cognitive subscore (r = 0.357, p = 0.004), physical subscore (r = 0.594, p < 0.001) and social subscore (r = 0.574, p < 0.001) as well as negative correlation between QoL and ABC scale scores (r = -0.443, p < 0.001). No correlation between the BBS and other scales was found (Table 3).

Table 2. Results of outcome measures at baseline and after 12-week exercise program

	Baseline Assessment Mean±SD	After Treatment Mean±SD	p values (Student t test)	
EDSS	4.62±1.29	4.54±1.39	0.410	
BBS	42.9±7.1	47.3±5.2	<0.001	
FIS-total(%)	42.7±15.7	37.2±18.2	0.060	
FIS- cognitive (%)	37.9±16.5	31.5±18.3	0.002	
FIS- physical 4 (%)	48.2±20.7	37.6±20.3	0.001	
FIS- social (%)	42.5±15.3	35.9±17.4	0.002	
ABC-S (%)	44.1±19.9	52.9±19.3	<0.001	
MUSIQOL	42.4±14.2	34.7±14.1	<0.001	

Abbrev.: EDSS. Expanded Disability Status Scale. BBS. Berg Balance Scale: FIS. Fatigue Impact Scale total, cognitive, physical, social; ABC_S. Activities Specific Balance Confidence Scale: MUSIQOL. Multiple Sclerosis International Quality of Life questionnaire

Variable	BBS	FIS-cog	FIS-soc	FIS-soc	FIS-tot	ABC_S	MUSIQOL	ED SS
1. BBS								
2. FIS-cog	0.128							
3. FIS-phs	0.148	0.707b						
4. FIS-soc	0.189	0.777b	0.850 ^b					
5. FIS-tot	0.174	0.747b	0.831b	0.919 ^b				
6. ABC_S	0.318a	-0.456b	-0.640b	-0.564b	-0.553b			
7. MUSIQOL	-0.083	0.357b	0.594 ^b	0.574 ^b	0.589 ^b	-0.443 ^b		
8. EDSS	-0.314a	0.031	0.170	-0.007	-0.043	-0.288a	0.219	

Abbrev.: BBS, Berg Balance Scale; FIS, Fatigue Impact Scale total, cognitive, physical, social; ABC_S, Activities Spisific Balance Confidence Scale; MUSIQOL, Multple Sclerosis International Quality of Lifi questionnaire; EDSS, Expanded Disability Status Scale. a=correlation significant at 0.05 level. b=correlation significant at 0.01 level

When the patients were assembled into groups based on EDSS scores, Group 1 involved 32% of patients with mild disability (n=13, EDSS \leq 3.5), and Group 2-, 58% (n=18, EDSS: 4.0-6.5) of patients with severe disability. No significant difference was observed between the groups in BBS (p=0.24), FIS total (p=0.31) and cognitive, physical and social subscores (p=0.14, p=0.21, p=0.64, respectively), ABC scale (p=0.11) and MusiQoL questionnaire (p=0.08).

According to the disease duration, the patients were classified into two groups. Group 1 involved patients with a disease duration of less than 10 years, and group 2-, patients with more than 10 years. There was no significant difference between the groups except for the baseline BBS scores (p=0.04), which was not significant at the 12th week assessment (p= 0.271).

Discussion

The major results of this study was that QoL, balance and fatigue improved significantly after home-based exercise training in MS individuals. However, disability status remained the same after the 12-week exercise program.

MS patients become more inactive due the unstable disease course and the effects on primary system. Fatigue and balance dysfunction have been the most common symptoms reported in MS, leading to lower QoL and functional capacity in these patients (27-29). Recent studies suggested regular physical activity for the solution of problems associated with inactivity and for improvement of QoL (30-34).

As it is well known that, training programs of three months or longer make it more likely to gain measurable cardiovascular, morphological and neural adaptations (35), therefore, our participants were admitted to a three-month training program focusing on balance and functional mobility. All of the participants showed improvements in QoL, fatigue, and balance functions after the home-based exercise program. Our findings are supported by Straud et al., who demonstrated that regular exercise might play an important role in achieving lower fatigue levels and higher activity levels in association with reduced fatigability (29).

While MS patients often report lower QoL than healthy individuals, improving QoL of MS population has become an

important goal of researchers and QoL assessments are increasingly popular as an important health outcome measures in MS (30-31). Although MS-specific questionnaires may assess QoL more effectively (13,26,36,37), studies are commonly applying generic QoL instruments (8,29,38). For this reason, we assessed QoL in MS individuals with a disease-specific questionnaire. MusiQoL, which validity and reliability of the instrument have been established in patients with MS (24). The mean MusiQoL score decreased from 42.4 to 34.7 by the end of the treatment with significant improvements in QoL. In addition to this, we found that improvement in balance correlated with improvement in QoL which might be explained by the increased functional ability and self confidence resulting in positive effects on the aspects of QoL such as social, physiological and cognitive factors. As MS was found in relation with balance dysfunction and loss of balance confidence, which led to functional limitations, dependency in activities of daily living (39), and increasing risk of falling or activity avoidance in MS patients (2), we assessed balance and balance confidence of the participants with two common scales: BBS and ABC scale. Baseline median score of the patients increased from 43 to 47, and from 44% to 53% by the end of the training, respectively. This change was found statistically significant and also a significant correlation was observed between the BBS and ABC-scale scores, which explained the relationship between functional balance abilities and balance confidence after the exercise training. Loss of confidence may affect functional ability of patients. Thus, the balance confidence seems to be an important part of balance evaluation to consider among MS individuals when the rehabilitation of balance and mobility are planned. The self-assessed balance confidence may also be a useful screening tool to identify persons with impaired balance and mobility (39).

In MS studies, an inverse relationship has been found between QoL and disability status (26,28). Unlikely, we did not observe any relationship between disability status and QoL; it may be speculated that QoL might be assessed independent from disease severity.

Excessive fatigue is one of the most common symptoms of MS. Fatigue can be caused by several factors such as physical, cognitive and social factors. Physical fatigue might be related to

muscle weakness, deconditioning, muscle hypertonus and respiratory muscle weakness that lead to higher energy consumption during activity (38). Psychological factors such as illness cognitions or perceptions may also contribute to fatigue and disability in MS. It was found that the illness perceptions of patients correlated with fatique and disability levels also for actual MS status, time since diagnosis, and remission status (40). Another study (41) also suggested that behavioral patterns may have a special importance to point when supporting patients to cope with fatique and disease-related impairments. For these reasons, we evaluated the fatigue level of the participants with FIS which has three components of fatigue such as cognitive, physical and social. After the statistical analysis, we found that while the patients did not show significant improvements in total scores of FIS, however they presented significant improvements in the subgroup scores of FIS after the exercise intervention, thus, fatigue has to be explained not only with the total aspects of fatigue, but also and preferably with the different components of fatigue. Additionally, we observed a relationship between MusiQoL score and FIS total and subgroup scores which highlights also the importance of cognitive, physical and social features of fatigue.

In the literature, a great number of exercise intervention studies have focused on positive benefits of physical activity on MS patients with low disability (13,25). There is a need for more information on the influence of physical activity on MS patients with higher disability. In our study 58% of patients with severe disability (EDSS scores=4.0-6.5), showed similar improvements in QoL, fatigue and balance functions compared to patients with mild disability (EDSS scores \leq 3.5). It might be related to the improved disability perception of patients after regular exercise which leads to enhanced functional ability (29).

Our study emphasize that MS individuals have great tendency to decrease their activity level which might start at the beginning of the disease or increase as disability status progressed. We found that MS patients with a disease duration of more than 10 years or with EDSS scores of 4.0 to 6.5 achieved similar improvements independent from their disease duration and disability status. Exercise training resulted in significant improvements in both patients with low and high disability levels. Therefore, the neurological rehabilitation professionals, who are specialized on this area, have to consider the benefits of exercise and physical activity for MS patients, independent from the disability status and disease duration, and encourage them to take part into an exercise program.

Acknowledgements

We are grateful to the patients of the Multiple Sclerosis Outpatient Clinic of Neurology Department for their participation in this study.

References

- Motl RW, McAuley E, Snook EM et al. Physical activity and quality of life in multiple sclerosis: intermediary roles of disability, fatigue, mood, pain, self-efficacy and social support. Psychol Health Med 2009; 14(1):111-24.
- Kelleher KJ, Spence W, Solomonidis S et al. Ambulatory rehabilitation in multiple sclerosis. Disabil Rehabil 2009; 31(20):1625-32.
- Hale L, Williams K, Ashton C et al. Reliability of RT3 accelerometer for measuring mobility in people with multiple sclerosis: pilot study. J Rehabil Res Dev 2007; 44(4):619-27.

- Kayes NM, McPherson KM, Taylor D et al. The Physical Activity and Disability Survey (PADS): reliability, validity and acceptability in people with multiple sclerosis. Clin Rehabil 2007; 21(7):628-39.
- Snook EM, Motl RW. Effect of exercise training on walking mobility in multiple sclerosis: a meta-analysis. Neurorehabil Neural Repair 2009; 23(2):108-16.
- Motl RW, Gosney JL. Effect of exercise training on quality of life in multiple sclerosis: a meta-analysis. Mult Scler 2008; 14(1):129-35.
- White LJ, McCoy SC, Castellano V, et al. Resistance training improves strength and functional capacity in persons with multiple sclerosis. Mult Scler. 2004;10(6):668-74. DOI: 10.1191/1352458504ms1088oa.
- Dalgas U, Stenager E, Jakobsen J, et al. Resistance training improves muscle strength and functional capacity in multiple sclerosis. Neurology 2009;73(18):1478-84.
- Freeman J, Allison R. Group exercise classes in people with multiple sclerosis: a pilot study. Physiother Res Int. 2004; 9(2):104-7. DOI: 10.1002/pri.307
- DeBolt LS, McCubbin JA. The effects of home-based resistance exercise on balance, power, and mobility in adults with multiple sclerosis. Arch Phys Med Rehabil. 2004; 85(2):290-7. DOI:10.1016 /j.apmr.2003.06.003.
- Storr LK, Sørensen PS, Ravnborg M. The efficacy of multidisciplinary rehabilitation in stable multiple sclerosis patients. Mult Scler. 2006; 12(2): 235-42. DOI: 10.1191/135248506ms1250oa.
- Lord SE, Wade DT, Halligan PW. A comparison of two physiotherapy treatment approaches to improve walking in multiple sclerosis: a pilot randomized controlled study. Clin Rehabil. 1998; 12(6):477-86. DOI: 10.1191/026921598675863454
- Romberg A, Virtanen A, Ruutiainen J. Long-term exercise improves functional impairment but not quality of life in multiple sclerosis. J Neurol. 2005; 252(7):839-45. DOI: 10.1007/s00415-005-0759-2.
- Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis: guideliness for reserach protocols. Ann Neurol 1983; 13(3): 227-31.
- Kurtzke JF. Rating neurological impairment in multiple sclerosis: an Expanded Disability Status Scale (EDSS). Neurology 1983; 33(11):1444-52.
- Goldman MD, Marrie RA, Cohen JA. Evaluation of the six-minute walk in multiple sclerosis subjects and healthy controls. Mult Scler. 2008; 14(3): 383-90. DOI: 10.1177/1352458507082607.
- Armutlu K, Korkmaz NC, Keser I, et al. The validity and reliability of the Fatigue Severity Scale in Turkish multiple sclerosis patients. Int J Rehabil Res. 2007; 30(1):81-5. DOI: 10.1097/MRR.0b013e3280146ec4.
- Fisk JD, Ritvo PG, Ross L, et al. Measuring the functional impact of fatigue: Initial validation of the Fatigue Impact Scale. Clin Infect Dis 1994a; 18(Suppl. 1): 79-83. DOI: 10.1093/clinids/18.Supplement_1.S79.
- Berg K, Wood-Dauphinee S, Williams JI, et al. Measuring balance in the elderly: preliminary development of an instrument. Physiother Can 1989; 41(6):304-11. 10.3138/ptc.41.6.304.
- Cattaneo D, Jonsdottir J, Repetti S. Reliability of four scales on balance disorders in persons with multiple sclerosis. Disabil Rehabil. 2007; 30; 29(24):1920-5. (DOI:10.1080/09638280701191859).
- Powell, LE, Myers AM. The Activities-specific Balance Confidence (ABC) Scale. J Gerontol Med Sci 1995; 50(1):28-34.
- Cattaneo D, Regola A, Meotti M. Validity of six balance disorders scales in persons with multiple sclerosis. Disabil Rehabil. 2006;30;28(12): 789-95.D0I:10.1080/09638280500404 289.
- Cattaneo D, Jonsdottir J, Zocchi M, et al. Effects of balance exercises on people with multiple sclerosis: a pilot study. Clin Rehabil 2007; 21(9): 771-81. DOI: 10.1177/0269 215507077602.
- MC Simeoni, P Auquier, O Fernandez, et al. Validation of the Multiple Sclerosis International Quality of Life questionnaire. Mult Scler 2008; 14:219-23. DOI:10.1177/1352458507080733.
- Taylor NF, Dodd KJ, Prasad D, et al. Progressive resistance exercise for people with multiple sclerosis. Disabil Rehabil 2006; 28(18):1119-26. (DOIi:10.1080/09638280500531834).
- Amato MP, Ponziani G, Rossi F, et al. Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. Mult Scler 2001; 7(5):340-4. DOI: 10.1177/13524585010 0700511.
- Benedict RH, Wahlig E, Bakshi R, et al. Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder, personality, and behavior change. J Neurol Sci 2005; 15; 231(1-2):29-34. DOI: 10.1016/ j.jns. 2004.12.009.

 Lobentanz IS, Asenbaum S, Vass K, et al. Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality. Acta Neurol Scand 2004; 110(1):6-13. DOI: 10.1111/j.1600-0404.2004.00257.x

Exercise Program in Multiple Sclerosis Patients

- Stroud NM, Minahan CL. The impact of regular physical activity on fatigue, depression and quality of life in persons with multiple sclerosis. Health Qual Life Outcomes 2009; 7:68. (DOI:10.1186/1477-7525-7-68).
- Benito-Leon J, Morales JM, Rivera-Navarro J. Health-related quality of life and its relationship to cognitive and emotional functioning in multiple sclerosis patients. Eur J Neurol 2002; 9:497-502. (DOI: 10.1046/j.1468-1331.2002.00450.x)
- Mitchell AJ, Benito-León J, González JM, et al. Quality of life and its assessment in multiple sclerosis: integrating physical and psychological components of wellbeing. Lancet Neurol 2005; 4(9):556-66. DOI:10.1016/S1474-4422(05)70166-6
- Motl RW, McAuley E, Snook EM, et al. Validity of physical activity measures in ambulatory individuals with multiple sclerosis. Disabil Rehabil 2006; 28(18):1151-6. (doi:10.1080/096 38280600551476).
- Dalgas U, Stenager E, Jakobsen J, et al. Fatigue, mood and quality of life improve in MS patients after progressive resistance training. Mult Scler. 2010; 16(4):480-90. 10.1177/1352458509360040.
- İyigün G, Aksu Yıldırım S, Snowdon N. Is Physiotherapy Effective in Improving Balance and Gait in Patients with Multiple Sclerosis?: A Systematic Review. Turkiye Klinikleri J Med Sci 2010; 30(2):482-93.

- Dalgas U, Stenager E, Ingemann-Hansen T. Multiple sclerosis and physical exercise: recommendations for the application of resistance-, endurance- and combined training. Mult Scler. 2008; 14(1):35-53. DOI: 10.1177/1352458507079445.
- Ozakbas S. [Quality of Life Assessments in Multiple Sclerosis]. Turkiye Klinikleri J Neurol 2004; 2(3):249-53.
- Ozakbas S, Akdede BB, Kösehasanogullari G, et al. Difference between generic and multiple sclerosis-specific quality of life instruments regarding the assessment of treatment efficacy. J Neurol Sci. 2007; 15; 256(1-2):30-4. DOI:10.1016/j.jins. 2007. 01.080.
- Sihvonen S, Kulmala J, Kallinen M, et al. Postural balance and selfreported balance confidence in older adults with a hip fracture history. Gerontology. 2009; 55(6):630-6. DOI: 10.1159/000240016.
- Mostert S, Kesselring J. Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. Mult Scler. 2002; 8(2):161-8. DOI: 10.1191/1352458502ms779oa.
- Jopson NM, Moss-Morris R. The role of illness severity and illness representations in adjusting to multiple sclerosis. J Psychosom Res. 2003; 54(6): 503-11. DOI: 10.1016/S0022-3999(02)00455-5.
- Skerrett TN, Moss-Morris R. Fatigue and social impairment in multiple sclerosis: the role of patients' cognitive and behavioral responses to their symptoms. J Psychosom Res 2006; 61(5):587-9. DOI:10.1016/ j.jpsychores.2006.04.018