THE EFFECT OF EXERCISE ON FATIGUE IN PATIENTS WITH MULTIPLE SCLEROSIS

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Abstract

The aim of this study is to show the effect of exercise on fatigue in patients with multiple sclerosis (MS). Exercise or remedial gymnastics is a commonly used non-pharmacological method of treatment of fatigue in patients with MS. A positive effect of exercise on the reduction of fatigue in patients with MS is expected. Data on patients and nature of the disease were obtained by reviewing medical documentation and patient survey feedback. The 62 patients who met the inclusion criteria filled out the MFIS questionnaire at the beginning and at the end of a one-month study. Individually-adapted relaxation, stretching, breathing, strength, coordination and balance exercises were implemented, as well as aerobic and neurophysiological exercises, 3 times per week (12 treatments). In the test group, fatigue which affects physical functioning was reduced averagely by 0.77, but the difference was not statistically significant (p=0.165). In the control group, the values were increased averagely by 0.23, but the difference was not statistically significant (p=0.338). Among the subjects who exercised, fatigue which affects cognitive functioning was reduced averagely by 0.90, but the difference was not statistically significant (p=0.224). In the control group, an increase of averagely 0.45 was recorded, but the difference was not statistically significant (p=0.365). Among the subjects who exercised, fatigue that affects patients' psychosocial functioning was reduced averagely by 0.10, but the difference was not determined (p=0.368). In the control group, fatigue was increased averagely by 0.16, but the difference was not statistically significant (p=0.323). In patients who exercised, the total score of MFIS was decreased averagely by 1.84, but the difference was not statistically significant (p=0.181). In the control group, an increase of 0.87 was recorded, however, not statistically significant (p=0.335). Physical exercise had an expected positive effect on fatigue measured by the MFIS questionnaire in all its aspects (cognitive, psychosocial and physical), as well as the total score, but considering the small number of subjects and a short period of research, the difference is not statistically significant.

***Key words**: multiple sclerosis, physical exercise, fatigue, rehabilitation*

Introduction

MS is an inflammatory demyelinating disease of the central nervous system which affects young adults. The main characteristic of MS are numerous demyelinating lesions of the central nervous system, i.e., plaques, after which the disease was named MS, due to gliotic sclerosis of lesions. In the beginning, it is usually manifested in acute neurological disturbances, i.e., relapses, which gradually completely or partially recede. This relapsing-remitting character is the main clinical characteristic of MS. In the beginning, the inflammatory demyelinating lesions are mainly localized in the white matter of the central nervous system, even though in the very beginning, and especially in the later stage of the disease, axonal and neuronal lesions occur (Brinar, 2009). Approximately 2-2.5 million people are affected by MS worldwide (Alajbegović & Denišlič, 2010; Milo & Kahana, 2010). The prevalence of the disease is variable worldwide depending on geography, race and nationality; thus, the incidence rate of the disease varies even in countries of the same latitude (Alajbegović & Denišlič, 2010; Soldo-Butković, 2013). A north-south gradient of prevalence of the disease exists the further you move from the equator and the prevalence rate is higher in the areas with predominantly white population. According to the studies, the Republic of Croatia is classified as the area of medium to high risk for MS, although it must be mentioned that the data are incomplete (Materljan & Sepčić, 2002; Alonso & Hernán, 2008; Brinar, 2009; Alajbegović & Denišlič, 2010). Regardless of the evident geographical north-south gradient, it should be noted that in almost each of these areas there is a region in which MS is significantly more prevalent. Such regions are called clusters. This again implies the thesis that MS is a disease influenced by genetic and environmental factors (Alonso & Hernán, 2008; Brinar, 2009; Alajbegović & Denišlič, 2010). Studies have shown that global prevalence of MS, and of autoimmune diseases in general, has increased in recent years. Incidence has increased particularly in women. Even though it is not a hereditary disease, MS shows significant family incidence. According to studies, about 20% of patients have at least one relative who is also afflicted by multiple sclerosis, whereas the risk of developing MS in first-degree relatives is increased by 3.4-5.13% (Alajbegović & Denišlič, 2010; Milo & Kahana, 2010). MS is more common in women, i.e., female to male ratio is 2:1. Over the last 50 years, this ratio has additionally increased and in some areas such as Canada, it exceeds 3.2:1. Such ratio is particularly prominent at an early age and decreases with patients' age, especially after the age of 50 (Brinar, 2009; D'hooghe, D'hooghe, & De Keyser, 2013). Life expectancy in MS patients is shortened averagely by 5-10 years, and the main causes of death are complications of the disease in 50% of the patients (Ebers, 2001; Milo & Miller, 2014). Etiology of the disease is still unknown. It is believed that the disease occurs due to the changed immune response in people with genetic predisposition, in interaction with some, not yet fully known, environmental factors. It has been proven that there is no single factor, but rather an interplay of multiple factors, thus, multiple sclerosis is considered a multifactorial disease. Possible causes for multiple sclerosis can be divided into external and internal factors. The most common opinion today is that the disease is caused by molecular mimicry. It seems that the risk of developing the disease is increased if a person with genetic predisposition contracts rubella or infectious mononucleosis (Brinar, Zadro, & Barun, 2007; Schafer, Kitze, & Poser, 2009). Fatigue is one of the most common symptoms of multiple sclerosis, occurring in about 80% of patients, whereas 55% of patients describe fatigue as one of the worst symptoms (Khan, Amatya & Galea, 2014). Fatigue in multiple sclerosis is different than fatigue in healthy population, it is hard to define, and thus one of the most challenging symptoms to treat (Hadjimichael, Vollmer, & Oleen-Burkey, 2008). Fatigue is considered to be one of the main causes of impaired quality of life among MS patients, independent of depression or disability. For many patients, fatigue is considered to be the single most debilitating symptom, surpassing pain and even physical disability. Fatigue also imposes significant socioeconomic consequences, including loss of work hours and in some instances, even loss of employment (Braley & Chervin, 2010). Causes for fatigue in multiple sclerosis are still unknown. It is assumed to be the result of mediated processes in the brain, characteristic for multiple sclerosis, such as demyelination and axonal loss, and a consequence of immune response. For the treatment of fatigue in multiple sclerosis, a combination of pharmacological and non-pharmacological treatment is recommended, encompassing a multi-disciplinary approach (Khan, Amatya, & Galea, 2014). Clinical practice guidelines suggest medication (e.g., Amantadine and Modafinil) and rehabilitation (e.g., exercise, energy or fatigue self-management education, and cognitive behavioral therapy) for managing fatigue (Asano & Finlayson, 2014). Even the term "fatigue" is used without standard definitions or means of measurement. Many studies fail to define fatigue, perhaps due to the assumption that the term is clearly known to all. Even among studies that define fatigue, there is a considerable range of definitions (Kluger, Krupp, & Enoka, 2013). The Multiple Sclerosis Council for Clinical Practice defines fatigue as „a subjective lack of physical and/or mental energy that is perceived by the individual to interfere with usual and desired activities". According to this definition, fatigue can have a mental and/or physical origin and it is subjective. Due to the subjectivity in describing fatigue as a symptom, questionnaires for self-assessment of fatigue are probably the most commonly used tools. Several scales for quantifying fatigue have been created to date. There are no objective diagnostic tests for primary central fatigue in multiple sclerosis because neither an objective definition nor clear biological markers for assessing and measuring fatigue exist. The assessment is based on self-assessment questionnaires – subjective questionnaires measuring the quality of life in patients with multiple sclerosis. The most commonly evaluated and used questionnaires measuring fatigue are the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS). In clinical practice, both of these tools are accessible and easy to use and MS patients consider them to be relatively easy to fill out. Both questionnaires measure general fatigue and are not used to differentiate central and peripheral fatigue. In both questionnaires, a patient answers questions related to fatigue on a numerical scale (Cantor, 2010). Rehabilitation as a complex procedure of re-training for activities of everyday and professional life, emotional and social stability, is an integral part of treatment of patients with multiple sclerosis. A rehabilitation plan is defined after assessing the functional status, precisely defining the disability and evaluating the impact of the disease on patient's life. Individual approach and rehabilitation programme are necessary for successful rehabilitation. The programme must be constantly adapted to patient's condition and psychological status since a patient can feel well and cooperate fully one day, and be generally weak and apathetic the next. Kinesitherapy is the most effective physical method in rehabilitation of patients with multiple sclerosis. During exercise performance, fatigue should be avoided by optimally balancing between activity and rest, performing the exercises in relief position, in water and air-conditioned space. The optimal time for exercise is the time of day when patients feel at their best and when medications have the greatest effect (Flachenecker, 2015). Before 1970, it was believed that any form of physical activity can cause fatigue and new problems for patients with multiple sclerosis, thus it should be avoided. However, over time, physical exercise has proven to be beneficial for patients in terms of reducing fatigue, increasing strength, endurance and quality of life (Bašić Kes, 2018). The aim of this study is to evaluate the effect of physical exercise in treatment of fatigue in patients with multiple sclerosis. Physical exercise or remedial gymnastics is one of the most commonly used non-pharmacological methods of treatment of fatigue in patients with MS. A positive effect of exercise on the reduction of fatigue in patients with MS is expected.

Material and Methods

The study was conducted from November 2018 to February 2019, in cooperation with Multiple Sclerosis Society Split at the Medical institution for physical therapy and rehabilitation Priska Med in Split.

Subjects

The study included 95 patients aged 18 years and older, with confirmed diagnosis of multiple sclerosis. The inclusion criterion was adequate cognitive function of MS patients, assessed by the score of 24 or higher on the Mini-Mental Test. The exclusion criteria were regular ambulatory rehabilitation, acute attacks of the disease 3 months prior to the assessment, taking medications for fatigue, cognitive deficit and unwillingness to cooperate. Out of the 95 patients tested, 62 met the inclusion criterion. To test the effectiveness of physical exercise on fatigue, patients were divided into 2 groups by using a sealed envelope method. The test group included 31 patients engaged in a 4-week exercise programme. The control group included 31 patients who were not engaged in exercise.

Methods

All subjects had been informed on the contents of the study before they were included and they had signed an Informed consent for participation in the study. The study was approved by the Commission of the Multiple Sclerosis Society Split. Demographic data and data on the type of MS, duration of the disease, time of the last relapse, taking medications for fatigue, receiving immunomodulation therapy and ambulatory rehabilitation were obtained by a questionnaire and by reviewing medical documentation. At the facilities of the Society, 95 patients filled out a questionnaire, and 68 patients took the Mini-Mental test. After the testing, 62 patients met the inclusion criterion. All patients in the test and the control group filled out the MFIS questionnaire at the beginning and at the end of the study which lasted for a month. The rehabilitation treatment included exercise 3 times per week over a 4-week period (12 treatments). Depending on the functional and clinical status of the patients, individually adapted relaxation, stretching breathing, strength, coordination and balance exercises were applied, as well as aerobic exercises.

Questionnaire

Modified Fatigue Impact Scale (MFIS) was used to assess the effect of rehabilitation on the reduction of fatigue in patients with MS. For the use in clinical practice and research, a shorter version of the FIS scale of fatigue impact (MFIS), which consist of 21 questions (Appendix 2), is recommended. MFIS is part of the MS Quality of Life Inventory. For each of the 21 questions, a patient gives a 0 – 4 answer, with 0 meaning never, 1 – rarely, 2 – sometimes, 3 – often, 4 – almost always. The analysis of data obtained by the questionnaire yielded results on the effect of fatigue on physical, cognitive and psychosocial functioning of the patient. The questionnaire includes 9 questions related to patient's physical functioning, and scores range from 0 to 36. Furthermore, the questionnaire includes 10 questions assessing the impact of fatigue on cognitive functions, with scores ranging from 0 to 40. Two questions refer to the impact of fatigue on patient's psychosocial functioning, with scores ranging from 0 to 8. Total score can be expressed as the sum of all three items, and the highest total score is 84. A standardized result of the MFIS total score for MS does not exist, but the higher the value, the greater the fatigue level (Mikuľáková et al., 2018).

Statistical analysis

For data processing and statistical analysis, the Statistica 10 (StatSoft Inc., Dell, USA) statistical package was used. All values of metric variables were presented as mean values ± standard deviation. The following tests were used: Chi-Square Test, and in case of an unfavourable distribution, Fisher's exact test. The testing of differences among the observed groups was done by T-test, and ANOVA was used to determine multiple factors. Before conducting the tests, normality was tested by Kolmogorov-Smirnov test. Statistical significance was set at $P<0.05$.

Results and discussion

Demographic and clinical characteristics of the test and the control group of patients with multiple sclerosis are presented in Table 1.

Table 1. Demographic and clinical characteristics of the test and the control group of patients with multiple sclerosis

Characteristics	Test group (n=31)	Control group (n=31)	P
Men, n (%)	6 (19.3)	7 (22.6)	
Women, n (%)	25 (80.7)	24 (77.4)	0.755
Age (years), $\bar{X}$± SD*	45.5 ± 10.9	50.5 ± 13.3	0.066
Disease duration years, $\bar{X}$± SD*	8.9± 5.7	12.3 ± 10.9	0.072
Type of disease			
RRMS, n (%)	24 (74.2)	28 (90.3)	0.047
SPMS, n (%)	8 (25.8)	2 (6.5)	
PPMS, n (%)	0 (0)	1 (3.2)	
Immunomodulation therapy YES	9 (29%)	10 (32%)	0.783
NO	22 (71%)	21 (68%)	

*$\bar{X}$ – mean value; SD – standard deviation; RRMS - relapsing-remitting form of multiple sclerosis; SPMS – secondary progressive form of multiple sclerosis; PPMS – primary progressive form of multiple sclerosis

The test group included 25 women (80.7%) and 6 men (19.3%). The control group included 24 women (77.4%) and 7 men (22.6%). The average age of patients in the test group was 45.5 years, with average standard deviation from arithmetic mean of 10.9, whereas the average age of patients in the control group was 50.5 years, with average standard deviation from arithmetic mean of 13.3. The difference in relation to the test group was not determined (p=0.066). The average disease duration in test group patients was 8.9 years (SD=5.7), whereas the average disease duration in control group patients was 12.3 years (SD=10.9), and the difference between the two groups was not statistically significant (p=0.072). In the test group, 24 subjects (74.2%) were affected by the relapsing-remitting form of multiple sclerosis, whereas 8 subjects (25.8%) were affected by the secondary progressive form of the disease. In the control group, 28 subjects (90.3%) were affected by the relapsing-remitting form of multiple sclerosis, 2 subjects (6.5%) were affected by the secondary progressive form of multiple sclerosis, whereas 1 subject (3.2%) was affected by the primary progressive form of the disease. The relapsing-remitting form of the disease was more common in the test group than the control group (p=0.047). In the test group, 9 subjects (29%) received immunomodulation therapy, as opposed to the 10 subjects (32%; p=0.783) in the control group. The comparison of mean value of the Modified Fatigue Impact Scale (MFIS) for test and control group patients before and after rehabilitation treatment is presented in Table 2.

Table 2. Comparison of scores of the MFIS questionnaire

	Test group		Control group			
	$\bar{X}$*	SD**	$\bar{X}$	SD	t	p^+
F MFIS 1#	23.03	7.22	19.23	8.36	-1.92	0.030
F MFIS 2#	22.26	6.69	19.45	8.64	-1.43	0.079
K MFIS 1	22.58	10.22	15.61	9.06	-2.84	0.003
K MFIS 2	21.68	10.11	16.06	8.74	-2.34	0.011
P MFIS 1	4.94	2.11	3.58	2.19	-2.48	0.008
P MFIS 2	4.84	1.98	3.74	2.00	-2.17	0.017
U MFIS 1	50.55	17.74	38.39	17.47	-2.72	0.004
U MFIS 2	48.71	17.12	39.26	17.22	-2.17	0.017

*mean value; ** standard deviation; # ordinal number of measurement: 1- before exercise, 2 – after exercise; F MFIS – physical function of the Modified Fatigue Impact Scale; K MFIS – cognitive function of the Modified Fatigue Impact Scale; P MFIS – psychosocial function of the Modified Fatigue Impact Scale

Mean value on the physical subscale of fatigue in the first phase of testing was higher by 3.8 in test group patients in comparison to control group patients, and the existence of a statistically significant difference was determined (p=0.030). The testing of mean value differences in the second phase of the testing did not yield a statistically significant difference (p=0.079). On the cognitive scale of fatigue impact, a difference was determined in mean values by 6.97 points, where a statistically significant higher value was determined among test group patients (p=0.003), and a difference in the same direction was also determined in the second phase of the testing (p=0.011). Test group patients had higher mean value on the psychosocial subscale in the first phase of the testing by 1.36 points in relation to control group patients, and a statistically significant difference was determined (p=0.008). A statistically significant difference was also determined in the second phase of the testing (p=0.017), where a higher mean value was determined among test group patients. The total score of the MFIS in the first phase of the testing was higher by 12.16 points in test group patients. The difference was statistically significant in the first (p=0.004) and the second phase of the testing (p=0.017). The effect of exercise on fatigue which affects patients' physical functioning is presented in Table 3.

Table 3. The effect of exercise on fatigue which affects patients' physical functioning

Group		$\bar{X}$*	SD**	difference	t	p⁺
Test	F MFIS 1	23.03	7.22	-0.77	0.99	0.165
	F MFIS 2	22.26	6.69			
Control	F MFIS 1	19.23	8.36	0.23	0.29	0.388
	F MFIS 2	19.45	8.64			

*mean value; ** standard deviation; ⁺T-test; F MFIS – physical function of the Modified Fatigue Impact Scale

Among patients who exercised, fatigue which affects physical functioning was reduced averagely by 0.77, but the difference was not statistically significant (p=0.165). In control group patients, who did not exercise, values of fatigue which affects physical functioning were increased averagely by 0.23, but the difference was not significant (p=0.338). The effect of exercise on fatigue which affects patients' cognitive functioning is presented in Table 4.

Table 4. The effect of exercise on fatigue which affects patients' cognitive functioning

Group		$\bar{X}$*	SD**	difference	T	p⁺
Test	K MFIS 1	22.58	10.22	-0.90	0.77	0.224
	K MFIS 2	21.68	10.11			
Control	K MFIS 1	15.61	9.06	0.45	0.35	0.364
	K MFIS 2	16.06	8.74			

*mean value; ** standard deviation; ⁺T-test; K MFIS – cognitive function of the Modified Fatigue Impact Scale

Among the subjects who exercised, fatigue which affects cognitive functioning was reduced averagely by 0.90, but the difference was not statistically significant (p=0.224). Among the control group subjects, values of fatigue on the cognitive subscale were increased averagely by 0.45, but the difference was not statistically significant (p=0.364). The effect of exercise on fatigue which affects patients' psychosocial functioning is presented in Table 5.

Table 5. The effect of exercise on fatigue which affects patients' psychosocial functioning

Group		$\bar{X}$*	SD**	difference	t	p⁺
Test	P MFIS 1	4.94	2.11	-0.10	0.34	0.368
	P MFIS 2	4.84	1.98			
Control	P MFIS 1	3.58	2.19	0.16	0.46	0.323
	P MFIS 2	3.74	2.00			

*mean value; ** standard deviation; ⁺T-test; P MFIS – psychosocial function of the Modified Fatigue Impact Scale

Among the subjects who exercised, fatigue which affects psychosocial functioning was reduced averagely by 0.10, whereas the difference was not determined (p=0.368). In control group patients, who did not exercise, values of fatigue which affects psychosocial functioning were increased averagely by 0.16, and the difference was not statistically significant (p=0.323). The effect of exercise on the total score of the Modified Fatigue Impact Scale (MFIS) is presented in Table 6.

Table 6. The effect of exercise on the total score of the Modified Fatigue Impact Scale

Group		$\bar{X}$*	SD**	difference	t	p⁺
Test	U MFIS 1	50.55	17.74	1.84	0.93	0.181
	U MFIS 2	48.71	17.12			
Control	U MFIS 1	38.39	17.47	0.87	0.43	0.335
	U MFIS 2	39.26	17.22			

*mean value; ** standard deviation; ⁺T-test; U MFIS – total score of the Modified Fatigue Impact Scale

In patients who exercised, the total score of the MFIS was reduced averagely by 1.84, but the difference was not statistically significant (p=0.181). In control group patients, the total score of the MFIS was increased averagely by 0.87, but the increase was not statistically significant (p=0.335).

According to studies dealing with the effect of exercise on fatigue, it can be stated that exercise can affect the reduction of fatigue in patients with multiple sclerosis (Heine et al., 2015; Soysal Tomruk et al., 2016; Andreasen, Stenager & Dalgas, 2011). The results of our research show an average reduction of 0.77 (first measurement 23.03±22.26, second measurement 19.23±19.45) of fatigue on the physical subscale among the subjects engaged in organized exercise, but the difference is not statistically significant (p= 0.165). The results in the control group indicate that the values of fatigue which affects physical functioning were increased averagely by 0.23 (first measurement 19.23±8.36, second measurement 19.45±8.64), but the difference was not statistically significant (p=0.338). The analysis of cognitive fatigue shows that fatigue was reduced in the test group averagely by 0.90 (first measurement 22.58±10.22, second measurement 21.68±10.11), but the difference was not statistically significant. Among the control group patients, the fatigue values on the cognitive subscale were increased by 0.45 (first measurement 15.61±9.06, second measurement 16.06±8.74), but the increase was not statistically significant. Among the test group patients, the values of fatigue on the psychosocial subscale were reduced by 0.10 (first measurement 4.94±2.11, second measurement 4.84±1.98), but the difference was not statistically significant. In the control group, fatigue values were increased by 0.16, but the increase was not statistically significant. In the test group, the total score of the MFIS was reduced by 1.84 (first measurement 50.55±17.74, second measurement 48.71±17.12), but the difference was not statistically significant. In the control group, the total score of fatigue was increased by 0.87 (first measurement 38.39±17.47, second measurement 39.26±17.22), but the increase was not statistically significant. Out of the three subscales, the greatest increase was recorded on the physical subscale in the test group (p=0.165). The results of this study are congruent with the results obtained in a study by Mikuľáková et al. in which, as a result of exercise, fatigue was reduced on all three subscales (physical, cognitive and psychosocial) and in the total score of the MFIS questionnaire in the test group, whereas in the control group, fatigue values were increased (Mikuľáková et al., 2018). Physical exercise can have a positive effect on the reduction of fatigue in patients with multiple sclerosis, but research findings are heterogenous and mostly related to short-term effects of exercise. Previous studies dealing with the assessment of the effect of exercise on fatigue used undefined types of exercise which produce different results (Asano & Finlayson, 2014). Various forms of exercise are used to assess the effect of physical exercise on fatigue in patients with multiple sclerosis. The effect of aerobic exercise on the reduction of fatigue is often investigated (Petajan et al., 1996; Rampello et al., 2007;). Among other forms of exercise, some studies describe the effect of aquatic exercise on the reduction of fatigue in patients with MS (Kargarfard et al., 2012), as well as general endurance exercise, and combination of endurance and aerobic exercises (Hourihan, 2015). Even though the results of this study are not statistically significant, they still indicate the existence of a positive effect of physical exercise on fatigue which affects patients' physical, cognitive and psychosocial functioning. Since fatigue is difficult to define and measure, further research is necessary which would implement self-assessment questionnaires of fatigue to determine the real effect of physical exercise on fatigue in patients with multiple sclerosis. Moreover, future research should explore a unique exercise programme aimed at reducing fatigue in patients with multiple sclerosis, which would specify precisely the intensity, duration and frequency of exercise that can affect the reduction of fatigue.

Conclusion

Among the subjects who exercised, fatigue that affects physical, cognitive and psychosocial functioning was reduced in comparison to the patients in the control group who did not exercise. Among patients who exercised, the total score of the Modified Fatigue Impact Scale was reduced in comparison to the patients in the control group. Physical exercise had the expected positive impact on fatigue, but considering the small number of subjects, short period of research and other limitations, the difference was not significant.

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UČINAK TJELOVJEŽBE NA UMOR KOD OBOLJELIH OD MULTIPLE SKLEROZE

Sažetak

Cilj ovog istraživanja je prikazati kako provođenje tjelovježbe utječe na umor među oboljelima od multiple skleroze (MS). Tjelovježba ili medicinska gimnastika jedna je od često primjenjivanih nefarmakoloških metoda liječenja umora u oboljelih od MS. Očekujemo pozitivan utjecaj tjelovježbe na smanjenje umora u pacijenata s MS. Uvidom u medicinsku dokumentaciju i anketiranjem pacijenata dobiveni su podatci o pacijentima i prirodi bolesti. 62 pacijenta koji su zadovoljili kriterije uključenja u istraživanje ispunili su MFIS upitnik na početku i na kraju istraživanja koje je trajalo mjesec dana. Provodile su se individualno prilagođene vježbe relaksacije, istezanja, disanja, snaženja, koordinacije i ravnoteže, aerobne vježbe i vježbe neurofiziološkog koncepta 3 puta tjedno (12 tretmana). U ispitivanoj skupini je došlo do smanjenja umora koji se odražava na fizičko funkcioniranje u prosjeku za 0,77, ali razlika nije statistički značajna(p=0,165). Kontrolna skupina bilježi rast vrijednosti u prosjeku za 0,23, ali razlika nije značajna (p=0,338). Među ispitanicima koji su provodili vježbe došlo je do smanjena umora koji se odražava na kognitivno funkcioniranje u prosjeku za 0,90, ali razlika nije statistički značajna (p=0,224). Kontrolna skupina bilježi rast u prosjeku za 0,45, ali razlika nije značajna (p=0,364). Među ispitanicima koji su provodili vježbe došlo je do smanjena umora koji se odražava na psihosocijalno funkcioniranje pacijenata u prosjeku za 0,10, dok razlika nije utvrđena (p=0,368). Ispitanicima kontrolne skupine za 0,16 te razlika nije statistički značajna (p=0,323). U pacijenata koji su provodili vježbe došlo je do smanjenja ukupne vrijednosti MFIS-a u prosjeku za 1,84, međutim razlika nije statistički značajna(p=0,181). U kontrolnoj skupini zabilježen je rast za 0,87, međutim porast nije statistički značajan (p=0,335). Tjelovježba je imala očekivani pozitivni utjecaj na umor koji smo mjerili s MFIS upitnikom u svim njegovim razinama (kognitivnoj, psihosocijalnoj i fizičkoj) kao i u ukupnom rezultatu, obzirom na mali broj ispitanika i kratak period istraživanja ta razlika nije statistički značajna.

Ključne riječi: *multipla skleroza, tjelovježba, umor, rehabilitacija*

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