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Effect of a six-week concurrent exercise (stretching and aerobic) and the consumption of tetra hydro cannabinol additive on fatigue severity level among female MS patients

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ABSTRACT

Background and Objectives: The purpose of this study was to evaluate the effect of six weeks of combined training (stretching - aerobic) and tetra Hydro canabinol on Quality of life and fatigue in middle aged women with multiple sclerosis referring to the MS Society of Mashhad was in 2013. **Materials and Methods:** After sampling and random assignment to the control group Combination training group and the experimental group of Tetra Hydro canabinol, all participants completed a questionnaire fatigue (FSS) and the Quality of Life Questionnaire (QOL-50) in pre-test. Then the control group had a 6-week break. Combination training group, for 6-week did aerobic exercise (15 minutes stretching exercises, 15 minutes running 60 to 70 percent of maximum heart rate) and the experimental group of Tetra Hydro canabinol used of cannabis seed. After the experimental period all subjects completed a questionnaire of fatigue and quality of life and the results were analyzed with SPSS software. **Results**: According to the results, the quality of life before and after six weeks of combined training (stretching - aerobic) was similar. But the fatigue of test group was significantly lower than the pre-test. 6 weeks of consumption of tetra hydro cannabinol affected on fatigue and with its consumption rate decreased fatigue. Quality of life increased after consumption of tetra hydro cannabinol. Fatigue after six weeks of combined training (stretching - aerobic) were less. **Conclusions:** According to the results of this research can be concluded that sports and tetra hydro cannabinol was beneficial for middle-aged women with multiple sclerosis and reduce their fatigue level and tetra hydro cannabinol consumption will also increase their quality of life

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INTRODUCTION

Multiple Sclerosis (MS) is prevalent among inflammatory and demyelinating diseases of the central nervous system. About 2.5 millions of people worldwide are afflicted with this disease and day in day out their population is added to [1]. In Iran, the prevalence of this diseases has been reported to be about 15-30 individuals per 100 thousand people. Over 40,000 patients in Iran are estimated to be currently afflicted with this disease [1]. Its prevalent is 2-4 folds among women comparing to men and its prevalence age is reported to be 20 to 40 years. It shows up at youth [2]. This disease would lead to body weakness, fatigue and kinetic disorders and, therefore, affects individual's performance.

One of the most common symptoms of this disease which leads to severe mental/spiritual discomfort is fatigue. Fatigue induced by MS, implies topical muscular tiredness as well as an overall body disturbance. The reason for this fatigue is not well known yet. Disruption in the transmission of waves from the cells without myelin, the presence of cytokines in plasma and cerebrospinal fluid may be some of its correlates [3]. Moreover, in patients suffering from MS, physical activities require more energy than ever before due to the damage to different brain areas. Muscles with spasticity contract against each other, and therefore more energy would be required to do a simple activity. This would result in fatigueamong patients. Moreover, most of the symptoms associated with this disease (depression, pain, insomnia and kinetic problems),do also lead to fatigue. About one third of patients suffer from this problem. About 50-60 percent of them refer to this problem as the most disturbing symptom of their disease [4,5]. Fatigue deeply affects other aspects of one's life. Through affecting

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an individual's capability of performing valuable life activities and roles, it negatively influences one's quality of life. Research findings have showed that these patients, as compared to healthy society members, have a lower quality of life [6]. A study conducted by Zifko (2003) in the U.S. indicated that 75-90 percent of patients afflicted with MS suffer from fatigue. 50-60 percent of patients reported that fatiguedisrupted different aspects of their life. This researcher also indicated that fatigue was the most significant factor which lowered life quality among MS patients despite its complicated mechanism [7].

A key problem in MS patients is weakness and limitation in movements which would result in fatigue. This issue is on the one hand due to the entanglement of motor areas of brain and spinal cord and on the other hand due to the inactiveness of patients. Among the other reasons for kinetic limitation are depression, low spirits, fear of falling down or fear of engagement in an activity. Lack of motion results in the shortening and weakening of muscles, bed sore and constipation. Therefore, being physically active, doing exercises fitted to this disease and doing daily activities as well as particular exercises can improve these patients' motion problems [8,9]. Recent years have witnessed a growing attention to the significant role of sports in MS patients' lives. A body of research has investigated the effect of physical activities and stretching exercises mixed with aerobic exercises for these patients. Some of the findings were indicative of the positive effects of physical activities on these patients. Dissimilar findings were obtained by some other research, however. In a study conducted by Newman et al. (200)with this concern, stretching exercise combined with aerobics led to reduced fatigue. In another research carried out by Rampello et al. (2007), an 8-week aerobic exercise led to an increase in the speed and distance of walking. It, however, did not seem to affect the severity of fatigue [11]. The primary goal of sports in this chronic disease has been stated by researchers to be the maintenance and improvement of one's performance [10].

In recent years, non-medical methods have attracted the attention of most patients including those afflicted with MS. These are known as supplementary treatments. Besides the benefits of MS patients' engagement in physical exercises, researchers have recently realized that consumption of cannabis extract (tetrahydrocannabinol pill) can be effective in softening muscle stiffness in MS patients. That is because cannabis extract or tetrahydrocannabinol has an anti-spasm effect and hence, improve their physical condition [12,13]. The main compound in cannabis plant is delta-9 tetrahydrocannabinol which is known as THS in short. Another active compound existing in this plant is cannabidiol or CBD. Both of these compounds are among cannabinoids and are categorized as mental stimulants. They exert their effects through particular receivers which proliferate in number in different parts of brain and body. Moreover, recently some researchers have maintained that consuming this plant can help the reproduction of neurons and can, consequently, be considered as an effective treatment for many muscular problems and a relief of MS concomitant pains especially for those who tolerate too much pain [13,14].

On the one hand, muscular spasticity and fatigue is inevitable for MS patients and if not controlled, it can harshly influence their health and quality of life. On the other hand, this disease is on the rise. Therefore, we decided to investigate the effect of physical exercises and the additive consumption of tetrahydrocannabinol on fatigue severity among female MS patients. Few researcheshave been conducted so far concerning the effect of consuming tetrahydrocannabinol additive on MS patients. However, since the effect of cannabis extract has been attested to in reducing muscular spasm and consequently in making up for one's fatigue among these patients, this matter is of a great significance and there is a need for comparing the effect of exercises and the herbal tetrahydrocannabinol medicine on fatigue severity in MS patients.

Methodology:

This research is of a semi-empirical pre-test/post-test type. There were two groups: one experimental and one control group. This study is considered as an applied research. Research population consisted of all women afflicted with multiple sclerosis who visited Khorasan Razavi MS Assembly. After the public announcement in the assembly and the primary enrollment of female patients who were eager to participate in the research, the required information, research procedures and possible hazards were explained to the subjects in a meeting where a neurologist was present. Subsequently, based on the information obtained from the demographic information form, disease, age, body mass index and …'s expanded disability status scale (EDSS), 30 of MS patients who consented to take part in the study and also met the inclusion criteria were selected through the purposive, convenient sampling method. The subjects were 20-45 year-old women afflicted with MS who were under medical care, without any modification in their medication and were passing the dormant stage of the disease. Their EDSS score was between 1 and 4. Besides that, they had not experienced physical exercises during the past 6 months.

Having been singled out, the subjects began to fill out the fatigue measurement scale. Then they were randomly assigned to two experimental groups: 10 patients privileged with combinational exercises (stretching and aerobic) and 10 patients consuming the additive tetrahydrocannabinol. 10 more patients acted as the control group. Fatigue Severity Scale (FSS) was created in 1988 by a neurologist called Krupp in order to measure the severity of fatigue in MS patients. This instrument is highly valid in measuring fatigue severity in MS patients.

FSS makes a rapid measurement in these patients. The overall score obtained from it is in accordance with a patient's severity of fatigue. It is quite well understandable to all patients and 98% of patients can respond to its questions. This scale contains 9 items each having a 1-7 score. Score 1 implies a strong disagreement with the matter and score 7 means one strongly agrees with the issue. The overall score is estimated through the division of the sum of scores by 9. This overall score is also between 1 and 7. 7 show the peak of fatigue while 1 indicates no fatigue. Individuals who experience MS-related fatigue score about 5.1 while those who do not experience fatigue score around 2.8. Filling out this questionnaire takes less than 5 minutes and patients are supposed to respond based on their past 2 weeks. The analysis of the retest between the two time spans (5 to 33 weeks) showed no significant difference in the same clinical group afflicted with MS. A very high internal consistency (.88) was established by Cronbach alpha for this test. The reliability of the test was established though the test-retest method (r=.83) (15). The measurement process in this research was as follows: first of all, the fatigue severity of each patient was estimated though FSS index. Then their means were estimated as the final score.

After the assignment of groups, the 6-week combinational exercise (3 sessions a week) was performed for 40 minutes per session in the experimental group. Each session was comprised of 15 minutes of static and stretching movements, 15 minutes of aerobic activities such as running as intensely as 50 to 60 percent of maximum heart rate and then 10 minutes of returning to the initial status. Before the aerobic exercises, 15 minutes were spent on stretching exercises of neck, shoulders chest, biceps/triceps brachial muscles, back muscles and lower limbs. Each stretching lasted for 30 seconds. The stretching exercise would last for 15 minutes (6, 91). Training on how to perform the exercises was provided face to face. Each physical exercise was initially performed once by the researcher and once againcorrectly by the subject in the presence of the researcher. Then the next sport technique would be introduced. In case one felt exhausted, the exercise would be immediately stopped and continue just after one's fatigue was removed.

In the other experimental group, consumption of the additive tetrahydrocannabinol began and continued for 6 weeks. In the first two weeks, 5 milligrams of the additive was consumed. Since the 3rd week, each week 5 milligrams were added to the amount of additive. In the 6th week, the amount reached 25 milligrams (122). After 6 weeks, again FSS was filled out by the subjects and their responses were recorded as the post-test results. During this 6-week period, the control group members promised not to engage in any regular physical exercise and to inform the researcher in case any kind of modification occurred in their medical program.

SPSS version 16 was used to analyze the data. Firstly, the normal distribution of the data was ensured through the use of Kolmogorov-Smirnov. Then, one-way ANOVA was used in the pre-test in order to homogenize the groups. Dependent-sample t-test was used to determine the effect of independent variables on dependent variables in each group. Repeated-measure t-test was used to examine the effect of independent variables on dependent variables between the experimental groups and the control. The significance level was set at $p<.05$.

Findings:

30 MS patients whose age ranged between 20 and 45 participated in this study. They were randomly divided in 2 experimental groups (10 subjects engaged in the combinational exercise, 10 subjects engaged in the consumption of additive tetrahydrocannabinol) and 1 control group (10 subjects). subjects statistical information including age, body mass index (BMI), length of disease and fatigue index are indicated in table 4.1,before the application of the independent variable.

Table 4.1: Central tendency, age distribution, length of disease, severity of fatigue of subjects before the intervention of independent variable

Max.	Min.	Mean ±SD	Groups	Variables
44	33	39/00±3/38	Combinational exercise	Age (years)
46	31	37/20±4/13	Additive consumer	
44	27	35/60±5/48	Control	
76	50	60/62±8/66	Combinational exercise	Weight (kilograms)
81	47	61/55±10/05	Additive consumer	
78	50	62/33±8/64	Control	
24/61	19/53	22/16±2/33	Combinational exercise	BMI (kg/m2)
25	19/56	22/96±2/25	Additive consumer	
29/48	19/53	23/47±3/74	Control	
11/00	2/00	4/88±2/80	Combinational exercise	Length of diseases (years)
12/00	0/5	5/95±4/33	Additive consumer	
22	0/5	6/66±7/04	Control	
5/89	4/11	4/94±0/52	Combinational exercise	Severity of fatigue (score)
5/33	3/00	4/63±0/75	Additive consumer	
6/33	4/11	4/57±0/32	Control	

Student's Paired t-test was used to determine the source of intra-group changes in each group as can be observed in table 4.2.

Table 4.2: The results of student's paired t-test of fatigue severity index in combinational-exercise group, additive consumer group and the control group in the pre- and post-tests

variable	group	stages		t-value	Significance level
		Pre-test SD ±mean	Post-test SD ±mean		
Fatigue severity (score)	Combinational exercise	4.94±0.52	3.18 0.82	7.500	0.001*
	control	4.57±0.32	4.44 0.39	2.066	0.084
	Additive consumer	4.64±0.75	3.72 0.88	5.28	0.001*

*Significance level is set at p<.05

Student's paired t-test (table 4.2.) indicated that the average alterations of fatigue severity index in the combinational exercise group was significant (p<.05). In other words, the fatigue severity index in the combinational exercise group decreased significantly from 4.94 in the pre-test to 3.18 in the post-test. It also revealed significant alterations of fatigue severity index in the additive consuming group (p<.05). In other words, the fatigue severity index of the second experimental group was reduced significantly from 4.63 in the pre-test to 3.72 in the post-test.Using the repeated-measure t-test, the interactive and inter-group changes in fatigue severity index of the two experimental groups as well as the control group in the pre- and post-tests are indicated in table 4.3.

Table 4.3: The results of repeated-measure t-test of fatigue severity index in the combinational exercise, additive consumer and control groups in the pre- and post-test

variable	group	stages		Interactive changes		Inter-group changes	
		Pre-test SD ±mean	Post-test SD ±mean	F value	significance	F value	significance
Severity of fatigue (score)	Combinational exercise	4.94 0.52	3.18 0.82	18.16	0.001*	0.989	0.388
	Additive consumer	4.63 0.75	3.72 0.88				
	Control	4.57 0.32	4.44 0.39				

*Significance level is set at p<.05

The results indicated in table 4.3 show that the inter-group changes in fatigue severity index were not significantly divergent in the three groups (p=.388). Nevertheless, the interactive changes of the groups and the stages are significant (p=.001). In other words, the profile of fatigue severity alterations in the groups does not follow the same pattern in the pre- and post-test.

Discussion and Conclusion:

The findings of the present research indicated that the mean changes of fatigue severity index had a significant decrease in the combinational exercise group. AsadiZaker et al. (2010) investigated the effect of sports on the speed of walking, severity of fatigue and quality of life among MS patients. Their research findings revealed that physical exercise managed to raise the speed of walking in these patients and also reduced their fatigue [16]. Sani'ee (2002) also observed that an 8-week physical exercising can lead to a significant difference in improving one's feeling of healthiness, increasing movement level and reducing fatigue severity and further advancement of the disease in the exercising group [17]. In a study conducted by Rampello et al. (2007) titled as the effect of stretching-aerobic exercises on motion fatigue among male and female MS patients, 95 patients with low to moderate disability level were randomly assigned to asportive group (47 subjects) and a control group (48 subjects). The testes in the sportive group took part in a 3-week monitored sport program which was followed by a 23-week house-held program. In the control group, patients continued their normal life. Research findings revealed that the 6-month stretching-aerobic exercise decreased women's and men's fatigue [11].

Disruptionin the performance of different body systems (including the respiratory and blood circulation systems) are among the reasons for fatigue. During physical exercises, the frequency of heart beats, the stroke volume of the left ventricle and consequently cardiac output are increased. Once the skeletal muscles activity is raised through sports and physical exercises, the blood flow entering the muscles would be also increased. Blood and oxygen are, therefore, more easily transmitted to muscular tissues. Moreover, once body's physiological activity is raised during sports, body would need more oxygen. And through an increased respiration and lung vital capacityalong with an increased alveolar ventilation this need is met. Eventually it can be stated that physical exercises result in reduced fatigue through improving the performance of body systems. Furthermore, the body of previous research shows that the less physically active an individual is, the less energy s/he would have. The lowering of physical activity can lead to the reduction of muscular mass and reduced

performance. It can, therefore, affect fatigue. However, doing sports results in enhanced strength, flexibility and power of muscles. It also helps the natural movements of joints which, in turn, helps to reduce fatigue (18, 19).

In addition, the findings of the present research indicated that changes in the mean fatigue severity index in the additive consuming group had a significant reduction. Recently, researchers have found out that cannabis extract (tetrahydrocannabinol pill) can be effective in relieving muscle stiffness (commonly painful in MS patients.Tetrahydrocannabinol or cannabis extract has an anti-spasm and anti-contraction effect and is considered as a real effective sedative to relieve muscular, rheumatism and nervous pain [20]. Vaney et al (2004) used pure cannabis extract called tetrahydrocannabinol for MS patients. They reported lowered spasm, more capaability of walking with less difficulty [21]. In the study conducted by Zajicek et al. (2003), their findings revealed that consuming this material leads to easier and less painful walking [22]. In another study, Notcutt et al. (2004) investigated the effect of a 12-week consumption of cannabis extract on improving muscle stiffness. To do this research, use was made of 2.5-25 milligrams oftetrahydrocannabinol pills or placebo. The researchers of this study realized that muscle stiffness was relieved in consumers of tetrahydrocannabinol twice as much as the placebo consumers [23].

Moreover, consuming this edible material can lead to the strengthening of body immune system as well as the regulation of hormones. All these factors can improve physical status and can reduce the severity of fatigue [14]. More recently, researchers have maintained that consuming this plant can cause the reproduction of neurons and can, therefore, be used as a beneficial treatment for muscular problems and relieving the pains associated with MS especially for those who tolerate too much pain [14].

No significant correlation was found between the effect of the 6-week combinational exercise (stretching/aerobic) and consuming the additive tetrahydrocannabinol on fatigue severity among MS patients. However, the interactive changes of the groups and stages were significant. In other words, the profile of changes in mean fatigue severity index followed no same pattern in the pre- and post-test stages. Among the reasons for the insignificant change of fatigue severity index in the combinational exercise group and the additive consuming group as compared to the control group are inadequate intensity and duration of the exercises as well as the inadequate dosage and length of consuming the additive. This suggests the need for further research in this area.

An overall examination of the findings of this research reveals that the exercising course and additive consumption managed to improve the severity of fatigue index among female MS patients to some extent. It needs to be reminded that physical exercises have infinite advantages for health. Women afflicted with MS are not exceptional. A regular and disciplined physical activity program can be one of the most effective, secure, economical and enjoyable ways of promoting the quality of life among women afflicted with MS. It can help to control the undesirable changes associated with MS. In addition, the findings indicated that consuming the additive tetrahydrocannabinol as taken in this study, can probably be effective in improving the quality of life among female MS patients through lowering fatigue severity.

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