

Efficacy Of Low Frequency Low Intensity Pulsed Magnetic Field On Fatigue In Persons With Multiple Sclerosis. A Randomized Controlled Trial.

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Abstract

Background: Fatigue is the most common symptom of multiple sclerosis (MS). It occurs in 75 percent to 95 percent of patients with MS. Fatigue occurs at all stages of the disease. The symptom is not related to the severity or to the duration of MS.

Aim:The aim of current study was to investigate the efficacy of pulsed Magnetic field on Fatigue in persons with Multiple Sclerosis.

Methods:Thirty persons with Multiple Sclerosis from both sexes represented the sample of this study. They were recruited from the outpatient clinics, Faculty of Physical Therapy, Cairo University and Multiple Sclerosis specialized clinic in the Neurology department, Faculty of Medicine, Cairo University. The person's age ranged from twenty to forty years. They were assigned randomly into two equal groups; the study group (GA) and the control group (GB).The assessment of fatigue is conducted before and after treatment for both groups by Fatigue Severity Scale(FSS) and Fatigue Assessment Scale(FAS). Assessment of Multiple Sclerosis symptoms was conducted before and after treatment for both groups by Expanded Disability Status Scale (EDSS). Study group (GA) treated by pulsed magnetic field (Low intensity and low frequency) applied on cranium in addition to a selected physical therapy program for fatigue for persons with Multiple sclerosis . Control group (GB) treated by the same program of treatment for Fatigue only as the (GA) without pulsed magnetic field. The duration of treatment was six weeks, three times weekly,and day after day.

Results:Comparison of the mean value of each variable pre and post treatment in each group revealed a significant improvement in all different parameters in both groups; however comparison between post results of both groups revealed that the study group (GA) showed a significant improvement compared to the control group (GB) in all different variables ($p < 0.05$ for all).

Conclusion: Application of pulsed magnetic field with low intensity and low frequency had a positive effect in decreasing MS fatigue.

Key Words:Multiple Sclerosis, Fatigue,Pulsed Magnetic Field, Fatigue SeverityScale, Fatigue Assessment Scale and Expanded Disability Status Scale.

1. Introduction:

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS) most commonly affecting young adults .Despite the bulk of research that has been done, the exact cause of MS remains unknown. The etiology of MS is most likely multi-factorial and caused by a complex interaction of auto-immune, environmental and multiple genetic factors [1].

Multiple sclerosis is a disease in which the immune system attacks the myelin sheath surrounding the axons of neurons in the CNS. Inflammation of myelin is associated with the formation of hard plaques (sclerosis) in the CNS that disrupts neural transmission and results in the loss of many functions of the body. Plaques may appear anywhere in the CNS, but there is a predilection for the optic nerves, corpus callosum, spinal cord, brainstem and cerebellum. Although Multiple sclerosis is generally considered a disease of the white matter, more recent research has shown that areas of demyelination coexist with diffuse axonal degeneration[2].

Fatigue is a subjective lack of physical and/or mental energy which is perceived by the individual or caregiver as interfering with usual and desired activities. Acute fatigue is defined as the onset or worsening of fatigue (within six weeks or less); chronic fatigue: (present more than 50% of the time, for more than six weeks) [3].

Fatigue presents as a chronic symptom, but it may also precede or accompany MS exacerbations. It is frequently the first symptom of MS. It is even reported as the only symptom of an acute relapse. It can severely affect the ability to perform activities of daily life and is a major reason for unemployment. It is associated with excess disability and a poor quality of life[4].

Transcranial Magnetic Stimulation is a non-invasive, nearly painless method of activation of human cortical neurons by applying a magnetic pulse over the scalp. It allows functional mapping of the human brain (brain mapping). It has proved to alter cortical activity in awake, behaving man and has provided considerable advance to studies of brain function in the last decade [5]. It was found that exposure to pulse; weak electromagnetic fields can alleviate symptoms of multiple sclerosis (MS)[6]. Improvements in fatigue and overall quality of life were significantly greater on the study group [7].

The aim of this work was to investigate the efficacy of pulsed Magnetic field on Fatigue in persons with Multiple Sclerosis

2. Materials and Methods:

2.1. Study Design

The current single-blind, randomized, controlled study was approved and issued by the Faculty of Physical Therapy Ethical Committee, Cairo University, Egypt. It followed the ethical research principles of the World Medical Association (WMA) Declaration of Helsinki for human subjects

2.2. Participants:

Thirty persons with MS from both sexes were recruited in this study from outpatient clinic, Faculty of Physical Therapy and multiple sclerosis specialized clinic in the Neurology department, Faculty of Medicine, Cairo University. They were diagnosed and referred by a neurologist. All patients were divided randomly by simple randomization through random number generator into two equal groups (A and B); each of them is composed of fifteen patients.

Inclusion criteria: Subjects were recruited with signed consent, definite diagnosis of MS and stable for at least four months, the age ranged from 20 – 40 years, general examination for patients were normal, patients could follow commands, patients were free from any secondary complication such as contractures or deformities, patients were ambulant.

Exclusion Criteria: The potential participants have been excluded if they meet one of the following criteria: Patients with any other neurological deficits or orthopedics abnormalities, patients who were unable to tolerate pulsed magnetic field application, patients with history of tumor, patients with psychiatric disorders, patients with cardiovascular diseases, patients who took drugs for fatigue (Amantadine).

2.3. Clinical Evaluation:

A brief explanation about the protocol of assessment was given to each person, all persons asked to read and sign a consent form before the conduction of study and condition of environment was nearly constant throughout the study. A detailed sheet was done for each person including: personal history, present history, past history, family history, phone number, diagnosis and neurological examination for each subject by the same neurologist. The following evaluations were performed for each person:

2.3.1. The fatigue assessment scale (FAS): The FAS is a fatigue questionnaire consisting of ten items: five questions reflecting physical fatigue and five questions for mental fatigue. Although these two aspects of fatigue are represented in the questionnaire, the FAS appeared to be unidimensional in a Dutch working population as well as a

representative sample of the general population [8]. The response scale is a five-point scale (one never to five always). Scores on the FAS can range from ten to fifty [8]. The following ten statements refer to how the patient usually feel. For each statement, the patient can choose one out of five answer categories, varying from never to always. one = Never, two = Sometimes; three = Regularly; four = Often; and five = Always.

2.3.2. The Fatigue Severity Scale (FSS): It is a scale used in the evaluation of fatigue that affects the body. A list of statements/questions is provided. These statements are related to the different aspects of fatigue and how it affects the body. One has to just rate the question/statements and not answer them. The rating given to these questions is used in determining the state of a person's health. While rating the questions, one should make use of the scale with numbers from one to seven. If a person strongly agrees with a particular statement, the rating of seven should be given. Strong disagreement is expressed by rating the question as one. Depending on one's own experiences, ratings between one and seven can be given. One cannot skip a particular question. It is mandatory to answer all questions to obtain a better understanding of fatigue. The sum total of ratings given to all questions is used to determine the degree or severity of fatigue [9]. The total score of 36 or above calculated using the scale indicates that a person is suffering from fatigue-related health problem. A score that is lower than 36 shows that the health is normal. Even if the FSS gives a rough idea of the possible health problems resulting from fatigue, the examiner cannot (and should not) make diagnosis on his own. There are many details and underlying causes behind a person exhibiting a particular or set of symptoms. A list of statements used for evaluating the health is presented below [10].

2.3.3. The Expanded Disability Status Scale (EDSS): EDSS is a rating scale that is frequently used for classifying and standardizing the condition of people with multiple sclerosis (MS). The EDSS provides a total score on a scale that ranges from zero to ten. The first levels 1.0 to 4.5 refer to people with a high degree of ambulatory ability and the subsequent levels 5.0 to 9.5 refer to the loss of ambulatory ability. The range of main categories include (0) = normal neurologic exam; to (5) = ambulatory without aid or rest for 200 meters; disability severe enough to impair full daily activities; to (10) = death due to MS. In addition, it also provides eight subscale measurements called Functional System (FS) scores. The levels of function within each category refer to the eight functional systems affected by MS [11].

2.4. Rehabilitation Program:

2.4.1. Treatment for Control group: included aerobic exercises bicycle training (Stair Master Stationary Bicycle) for 15 minutes and treadmill training (EN-Motion treadmill 230 V) for 10 minutes with rest 10 minutes by in between including breathing exercises (Deep diaphragmatic breathing exercises) [12][13]. Each person was treated for 18 sessions, three times/week, 35 minutes / session.

2.4.2. Treatment for Study group:

The persons received pulsed magnetic therapy followed by the physical therapy program of fatigue which conducted for the control group by the same physical therapist. Pulsed magnetic therapy was performed by using ASA Magnetic Field for magnetotherapy, its model is Automatic PMT Quattro pro. Serial number is 00001543. All persons were instructed about equipment and its effect, the application procedure was explained to all persons, the persons sat on a chair with comfortable heights and cranial solenoids would be positioned where the whole head of the patient would be centered inside in the middle area, the equipment was calibrated and programmed before starting the session. Parameters used in the program were: Time of treatment 20 minutes, intensity (two Gauss) and frequency (one Hz) [14].

2.5. Statistical design: The statistical analysis was conducted by using statistical SPSS Package program version 25 for Windows (SPSS, Inc., Chicago, IL). The following statistical procedures were conducted:

Descriptive statistics: The mean and standard deviations.

Inferential statistics: By using t-test (test of difference), before and after physical therapy program for each group and between both groups A and B.

The level of significance for all statistical tests was set at ($P \leq 0.05$) [15].

3. Results:

3.1. General characteristics of the patients in the study and the control groups:

General characteristics of the persons are summarized in (Table 1). The two groups were homogeneous without statistically significant difference between them regarding age, sex distribution, disease course and

distribution. Also they were homogeneous regarding duration of illness and time from last attack without statistically significant between the both groups.

Table 1. Patient characteristics in both groups

Item	Study group (GA)	Control group (GB)	T-value	P-value
	Mean \pm SD	Mean \pm SD		
Age	30.37 \pm 6.96	28.2 \pm 5.91	0.93	0.367
Duration of illness (months)	21.53 \pm 1.94	22.20 \pm 1.67	0.23	0.814
Last attack (months)	6.33 \pm 1.13	5.33 \pm 1.13	0.82	0.425
Sex (Males & females)	6/9	10/5	(X ² = 0.14)	0.7
Main problems				
	Sensory	4/15	8/15	
	Motor	10/15	6/15	
	Sensorimotor	1/5	1/15	
Course	Remission& relapse	12/5	15/15	
	Primary progressive	1/15	0/15	
	Secondary progressive	2/15	0/15	

3.2 Comparison between the mean values of control and study groups, regarding FAS,FSS, and EDSS before and aftertreatment:

There was no statistically significant difference between the study and control groups regarding FAS, FSS and EDSS before treatment (P >0.05).

There was a statistically significant improvement of FAS,FSS and EDSS post-treatment in the study group (P < 0.05). And also there was a statistically significant improvement of FAS,FSS and EDSS post-treatment in the control group (P < 0.05). There was a statistically significant improvement of study group compared to control group post- treatment (P < 0.05) (Table 2).

Table 2. Comparison between the mean values of control and study groups, regarding FAS, FSS, and EDSS before and after treatment

Items	Groups	Study group (GA)	Control group (GB)	P-value
		Mean \pm SD	Mean \pm SD	
I-Fatigue Assessment Scale (FAS).	Pre-treatment	32.53 \pm 6.17	37.20 \pm 6.71	0.08
	Post-treatment	24.40 \pm 3.98	36.8 \pm 6.81	0.0001*
		P=0.0001*	P=0.028*	
II-Fatigue Severity Scale (FSS)				

Pre-treatment	50.93±8.66	51.40±7.95	0.868
Post-treatment	30.07±10.41	5.13±7.80	0.0001*
	P=0.0001*	P=0.041*	
III- Expanded Disability Status Scale (EDSS)			
Pre-treatment	5.067±0.961	4.933±0.884	0.685
Post-treatment	3.667±0.961	4.46±0.743	0.0001*
	P=0.0001*	P=0.014*	

4. Discussion:

The present study was conducted to investigate the efficacy of pulsed magnetic field in addition to a selected physical therapy program applied on fatigue for persons with Multiple sclerosis.

The post treatment results of this study revealed significant improvement in the mean values of the measuring variables of the control group which received a selected physical therapy program which proved the validity of the physical therapy techniques in treatment of Fatigue for persons with MS.

The significant improvement obtained in the post-treatment mean values of the measuring variables of control group may be attributed to the effects of aerobic exercise which increase overall physical activity and cardiovascular effort, prevent general muscular weakness and reduce health risks due to deconditioning and disuse. The few published studies of aerobic training with people with MS with Fatigue have shown beneficial effects at a physiological level in terms of aerobic capacity, physical fitness, and improved mood[16].

The significant improvement obtained in the post-treatment mean values of the measuring variables of control group agreed with Mostert and Kesselring who revealed that treadmill training and other forms of aerobic exercises in MS patients with mild to moderate disability is helpful and improved balance, the speed and endurance of walking, reduced fatigue and consequently; provided some positive effects on these patients' overall quality of life[17].

The main findings of the current study confirmed that pulsed magnetic field combined with a selected physical therapy program for six weeks had a positive effect on Fatigue in persons with MS. The study group (GA), which was treated by pulsed magnetic field in addition to selected physical therapy program showed greater significant improvement percentage in all clinical features and different aspects of Fatigue regarding FAS, FSS and EDSS than the control group (GB)

There is growing evidence in the literature for a beneficial effect of transcranial magnetic stimulation on different MS symptoms such as fatigue, bladder control, spasticity and quality of life [18]. who reported a reduction of spasticity by magnetic stimulation over the thoracic myelon while Sandyk, who demonstrated that weak magnetic field help in resolution of dysarthria, progressive cognitive improvement, improve body image perception, dual-task performance, resolution of L'hermitte's sign and improved alexia[19].

The results of the current study agreed with Lappin et al., in which all MS patients participated in his study experienced improvement in fatigue. Remarkably, patients noted that several months after initiation of treatment with electromagnetic fields they were able to recover, after a short period of rest, from fatigue which followed increased physical activity after receiving a course of treatments with picotesla flux electromagnetic fields (EMFs), which were applied extracranially. These observations suggest that replenishment of monoamines stores in neurons damaged by demyelination in the brainstem reticular formation by periodic applications of picotesla flux intensity EMFs may lead to more effective impulse conduction and thus to improvement in fatigue including rapid recovery of fatigue after rest[6].

The results of the current study also agreed with Gaede et al., who conducted a study on 26 MS-patients underwent eighteen sessions of rTMS over a period of six weeks to evaluate safety and efficacy of rTMS on Multiple Sclerosis patients. The effect on fatigue was evaluated with the Fatigue Severity Scale (FSS), the Modified Fatigue Impact Scale (MFIS) and a Visual Analogue Scale (VAS) of fatigue. They concluded that rTMS is safe and well tolerated in MS patients with structural brain lesions and have a positive influence on fatigue in Multiple sclerosis patients[20].

The results of the current study of the study group also agreed with Joachim et al., who demonstrated a beneficial effect of pulsed electro magnetic field therapy on MS fatigue. There was a statistically significant benefit for treated patients after twelve weeks. And they revealed that MS patients suffering from MS fatigue can benefit from electromagnetic field therapy which agree with the results of this study, but time of application of TMS in the current study was more time, twenty minutes compared to eight minutes in the study of Joachim et al., [21].

The results of the current study of the study group also agreed with Pia Amato and Portacci who revealed that 39 severely disabled patients with history of chronic relapsing-remitting multiple sclerosis (MS) began to experience improvement in symptoms within 24 hours after they received experimental treatment with picotesla electromagnetic fields (EMFs). The patients continued to receive one to two EMFs treatments per week and during the following six months, EMF made a dramatic recovery with resolution of diplopia, blurring of vision, dysarthria, ataxia of gait and bladder dysfunction as well as improvement in fatigue, heat tolerance, mood, sleep, libido and cognitive functions which agree with the results of this study according to fatigue problem [22].

In contrast to the results of present study Mostert and Kesselring who conducted a randomized controlled trial with a small sample size, showed that pulsed magnetic field therapy was not effective in reducing fatigue in MS subjects, as measured with FSS and VAS. Most of these studies published in the literature are based on small sample sizes [23].

Maria and Giovanna contradicted with the results of the present study as they stated that exposure to a low frequency magnetic field, has no advantage over sham exposure in reducing the impact of fatigue. Each group received both sham therapy and magnetic field therapy with a wash-out period of five months. Subjects were treated for 24 min per session, three times per week, for eight weeks [24].

Combined pulsed magnetic field with aerobic exercises results in the current study agreed with Francesco et al., who investigated whether the combination of transcranial magnetic stimulation and a program of aerobic exercises (treadmill training) can improve motor disability in MS patients. In a double-blind, sham-controlled trial, thirty participants were randomized to three different interventions: transcranial magnetic stimulation plus aerobic exercises, sham stimulation plus aerobic exercises, and transcranial magnetic stimulation alone. Before and after two weeks of treatment, measures of spasticity through the modified Ashworth scale (MAS) and fatigue through the Fatigue Severity Scale (FSS). Results revealed that transcranial magnetic stimulation plus aerobic exercises reduced MAS and FSS scores, TMS alone caused a reduction of the MAS score and FSS scores, while none of the measured scales showed significant changes after sham TMS plus aerobic exercises. TMS associated with aerobic exercises is a promising tool for reduction of spasticity and fatigue and motor rehabilitation of MS patients [25].

Liboff and Jenrow, demonstrated that pulsed magnetic field (PMF) induces currents in exposed tissue, which flow predominantly in the intercellular space and influencing the ionic motion across the cell membrane. PMF affect the distribution of ions across the cell membrane, thus accelerates the reestablishment of normal potentials and accelerates the rate of healing [26]. Magnetic field found to interact with the living cells influencing ATP production, increasing the oxygen supply and the nutrients via the vascular system and helping rebalance the distribution of ions across the cell membrane through influencing the membrane permeability and ionic motion [27].

5. Conclusion: The best modalities to decrease fatigue in persons with multiple sclerosis, combination of pulsed magnetic field and aerobic exercises is better than aerobic exercises alone.

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