Clinical Neurology and Neurosurgery 149 (2016) 171–174

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Evaluation of pulsing magnetic field effects on paresthesia in multiple sclerosis patients, a randomized, double-blind, parallel-group clinical trial

Daryoush Afshari (MD)[a], Nasrin Moradian (MD)[a,*], Majid khalili (MD)[a], Nazanin Razazian (MD)[a], Arash Bostani (MD)[a], Jamal Hoseini (MSc)[b], Mohamad Moradian[a], Masoud Ghiasian (MD)[c]

[a] Department of Neurology, Imam Reza Hospital, College of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Islamic Republic of Iran
[b] Department of Biostatistics & Epidemiology, Kermanshah University of Medical Science, Kermanshah, Islamic Republic of Iran
[c] Department of Neurology, Hamadan University of Medical Sciences and Health Services, Hamadan, Islamic Republic of Iran

ARTICLE INFO

Article history:
Received 30 November 2014
Received in revised form 9 August 2016
Accepted 14 August 2016
Available online 16 August 2016

Keywords:
Magnet therapy
Multiple sclerosis
Paresthesia

ABSTRACT

Objectives: Evidence is mounting that magnet therapy could alleviate the symptoms of multiple sclerosis (MS). This study was performed to test the effects of the pulsing magnetic fields on the paresthesia in MS patients.
Patients and methods: This study has been conducted as a randomized, double-blind, parallel-group clinical trial during the April 2012 to October 2013. The subjects were selected among patients referred to MS clinic of Imam Reza Hospital; affiliated to Kermanshah University of Medical Sciences, Iran. Sixty three patients with MS were included in the study and randomly were divided into two groups, 35 patients were exposed to a magnetic pulsing field of 4 mT intensity and 15-Hz frequency sinusoidal wave for 20 min per session 2 times per week over a period of 2 months involving 16 sessions and 28 patients was exposed to a magnetically inactive field (placebo) for 20 min per session 2 times per week over a period of 2 months involving 16 sessions. The severity of paresthesia was measured by the numerical rating scale (NRS) at 30, 60 days. The study primary end point was NRS change between baseline and 60 days. The secondary outcome was NRS change between baseline and 30 days.
Results: Patients exposing to magnetic field showed significant paresthesia improvement compared with the group of patients exposing to placebo.
Conclusion: According to our results pulsed magnetic therapy could alleviate paresthesia in MS patients .But trials with more patients and longer duration are mandatory to describe long-term effects.

1. Introduction

Multiple sclerosis is a chronic inflammatory debilitating disease of central nervous system (CNS) that mainly affecting subjects aged between 15 and 50 years. It has severe impact on patients and their families. Paresthesis is one of the most common presenting symptoms in Multiple Sclerosis [1,2]. About 40% of the patients reported that such symptoms had a serious adverse effect on daily activities. Painful Paresthesis leads to avoidance of any triggering activities [3]. Since it can have significant impact on quality of life, it needs to be treated appropriately. Medications that are used to treat paresthesia include carbamazepine, gabapentine and three cyclic anti-depressants [4].

Pharmacologic or rehabilitative treatments can treat MS symptoms such as paresthesia, spasticity and fatigue to a variable extent but management is quiet not ideal; therefore, the development of more effective symptomatic therapies remains a critical objective of MS care [5]. Patients with MS are widely using complementary and alternative medicine treatments, similarly to patients with other chronic diseases, yet the data concerning their effectiveness and safety is limited [5]. Pulsed electromagnetic field therapy (PEMFT), is a restorable technique most commonly used in the field of orthopedics for the treatment of non-union fractures, failed fusions, congenital pseudarthrosis and also for wound healing acceleration, alleviation of pain [6]. A large number of scientific and

* Corresponding author at: Department of Neurology, Faculty of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Islamic Republic of Iran.
E-mail address: moradiannasrin60@yahoo.com (N. Moradian).

http://dx.doi.org/10.1016/j.clineuro.2016.08.015
0303-8467/

Table 1
Baseline demographic and clinical characteristics.

Baseline characteristics	magnet group	placebo group	Total	P-value
Age (year) (Means ± SD)	37.88 ± 9.59	39.65 ± 10.67	38.52 ± 9/93	0.53
Female, N (%)	24(68.6)	16(64)	40(66.7)	0.58
Duration of disease (years) (Means ± SD)	10.31 ± 6.14	6.94 ± 5.12	9.14 ± 5.97	0.059
NRS(Means ± SD)	5.63 ± 1.96	5.45 ± 1.31	5.54 ± 1.63	0.38

SD: standard deviation.

clinical studies reporting that PEMFT help in bone unification, the reduction of pain, edema, and inflammation, and increasing blood circulation and stimulating the immune and endocrine systems [6]. Previous results revealed that Magnet therapy could alleviate the symptoms of MS, but that the effects were modest and required further confirmation [7]. The mechanisms by which magnets might relieve MS symptoms have not been conclusively identified or proven. Previous studies have shown electromagnetic field effects on CNS in the following areas: [1] altered calcium transport across cellular membranes —which may facilitate axonal conduction in brain damage caused by demyelination, [2] altered release of melatonin from the pineal gland, and [3] local or loco regional immunomodulatory action [8]. Although there have already been several anecdotal positive reports of effect of electromagnetic field on MS symptoms, no placebo controlled, double-blinded study is currently available in the literature investigated the effect of electromagnetic fields on MS paresthesia .This study was performed to test the effects of the pulsing magnetic fields on the paresthesia in MS patients.

2. Methods

This study was performed as a randomized, double-blind, parallel-group clinical trial during the April 2012 to October 2013. Patients with clinically definite MS who were admitted to outpatient MS clinic of Imam Reza Hospital; affiliated to Kermanshah University of Medical Sciences, Iran were included in this study. The informed consent obtained from all the patients. Kermanshah University of Medical Sciences approved the protocol of the study. The patients were included based on the following inclusion and exclusion criteria.

2.1. Inclusion criteria

1. Diagnosis of multiple sclerosis according to 2005 McDonald's criteria [9]. 2) History of paresthesia (defined as an abnormal sense of itching, prickling, tingling, burning and numbness in the limbs) or other parts of the body for at least 3 months. 3) Patients who had a numerical rating scale score of 4 or more. The NRS is a self-report estimate of paresthesia intensity measured on an 11-point Likert scale (0 = absent, 1–3 = mild, 4–6 = moderate, 7–10 severe) [10].

2.2. Exclusion criteria

1)Pregnancy, lactation or inability to use contraceptives throughout the study regarding females in childbearing ages. 2) Suffering from ischemic pain and other types of pain unrelated to multiple sclerosis such as phantom pain due to amputation, arthritis,peripheral neuropathy or cervical radiculopathy. 3) No MS exacerbations (defined as episodes of focal neurological disturbance lasting more than 24 h, without an alternate explanation, and with a preceding period of clinical stability lasting at least 30 days [11]) for one month prior to the study. 4) patients who have pacemaker or other metallic internal devices.

Table 2
Mean scores of numerical rating scale in follow up period.

	Mean score of NRS			P-value
	baseline	30th day	60th day	
Magnet	5/63 ± 1/96	4/97 ± 1/96	4/37 ± 2/03	0.001
placebo	5/45 ± 1/31	4/75 ± 1/55	4/3 ± 1/86	0.003

3. Procedure

By a computer generated randomization schedule, included patients were randomized as follows: the first group was exposed to a magnetic pulsing field of 4 mT intensity and 15-Hz frequency sinusoidal wave for 20 min per session 2 times per week over a period of 2 months involving 16 sessions. And the second group was exposed to a magnetically inactive field (placebo) for 20 min per session 2 times per week over a period of 2 months involving 16 sessions. Subjects were exposed to a pulsing magnetic field produced by the MAGNETOMED 7200(medical Italia) .This device includes a couch in aluminium with 2 highly sliding tracks and 2 cylinders with 60 cm diameter and 30 cm large for total body treatment, covered with imitation leather. Investigators and patients were blind to the treatments. Both group (active, non-active) did not any specific sensations when the device was on or off. A person who turned off or on the device was differ from investigator performed Follow-up visits and data collection and analysis. Patients allowed to remain on their current regimens but could not add any analgesics or treatments. The outcome was subjective paresthesia as assessed by the NRS [7], were rated daily by patients. Patients' daily ratings of paresthesia were registered by researcher for calculation of mean scores at the beginning of the trial and at 30, 60 days during the trial. The study primary end point was NRS change between baseline and 60 days. The secondary outcome was NRS change between baseline and 30 days. The incidence and severity of adverse events were tabulated throughout the study.

4. Statistical analysis

Patient's demographic and clinical information were recorded in a predesigned checklist. The data was analyzed with Statistical Package for the Social Sciences (SPSS) software version 19. Demographic variables and efficacy parameters of two groups were compared. Descriptive statistics were used to report variables of each medication group and also for total participants. Chi square test was employed to test the association of study characteristics between the two groups for categorical variable. Means were compared by the Student's *t*-test. Comparison for paresthesia score on NRS across time in both groups was carried out using Paired *t*-test. Results were reported as mean ± standard deviation (SD) and statistical significance was recognized at p values < 0.05.

5. Result

A total of 63 patients with MS were randomized. Three subjects dropped out of the study.

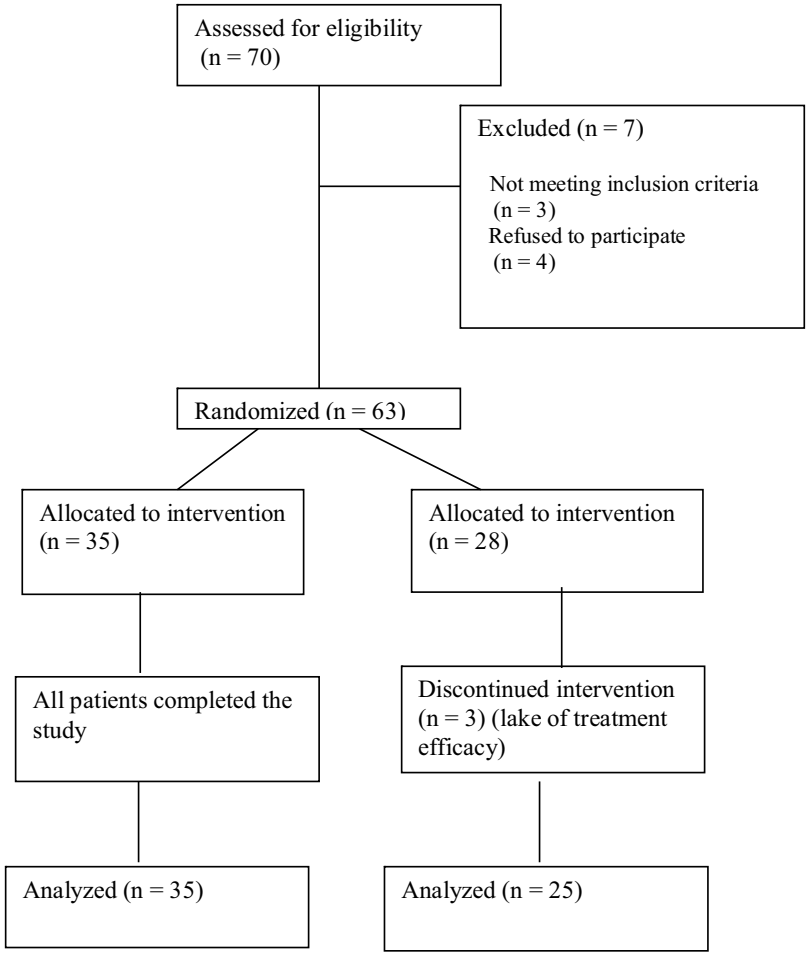

Fig. 1. Consort flowchart.

A flow chart of patient enrollment and disposition is provided in Fig. 1. 20 (33.3%) of the patients were males and 40(66.7%) females. Mean age was 38.52 +/− 9.93 years (19–63 years); mean disease duration was 9.14 +/− 5.97 years (1–20 years). All of the patients had a relapsing-remitting course. The demographic and clinical characteristics of the MS patients were shown in Table 1. There was no significant difference between baseline clinical and demographic characteristics of the different treatment groups (Table 1) parenthesis scores (NRS) were slightly higher in the magnet group compared to the placebo group, but this effect did not reach statistical significance (P = 0.38). Improvement for evaluated outcome measure was demonstrated in the both group (Table 2). The differences from baseline of both groups were compared over time: after 30 days of treatment, end of treatment (Table 3). Comparison of difference mean scores of paresthesis between the two groups indicated significant superiority of magnetic field therapy over placebo (Table 3). No adverse events were reported by patients in the both group.

Table 3
Difference mean scores of numerical rating scale in follow up period.

	difference mean score of NRS	
	30th day	60th day
Magnet	1.34 ± 1.13	1.94 ± 1.47
placebo	0.7 ± 0.73	1.15 ± 1.26
p-value	0.027	0.049

6. Discussion

In this double blind randomized placebo-controlled trial we demonstrated a statistically significant advantage for the magnet treatment group concerning an effect on the NRS over a 2-month period. Although both groups showed a decrease of paresthesia over the intervention time, NRS score was significantly lower in the magnet than in the placebo group 2 months later.

There is increasing evidence in the publications about a beneficial effect of magnetic field therapy on a variety of MS symptoms, such as fatigue, bladder control, spasticity, and quality of life [12]. Between 1992 and 1999, Sandyk reported cases of recovery from different MS symptoms by extra cranially applied electromagnetic field of 7.5 picotesla (7.5 × 10–12 T) at a frequency of 4–5 Hz [13–26]. In 2002, in a study on 76 MS patients conducted by Brola et al. after 21 days of pulsed magnetic fields therapy, the quality of life of the patients was seen to have improved significantly comparing with a control group ($p < 0.01$), especially with regard to their mental condition, muscle tone, dysesthesia and painful sensations; moreover, no side-effects were recorded [27]. Lappin et Al performed a placebo-controlled, double-blind, multicentre pilot study on 117 patients. Their Subjects were treated with an active or placebo device for four weeks. The device was taped to the skin 24-h a day over the brachial plexus. Study results demonstrated statistically significant improvements in MS-related fatigue and overall quality of life, more ambiguous results for spasticity, and no effects for bladder control. The authors concluded that the effects were modest and required further confirmation [7]. In contrast, results

of Mostert and Kesselring study did not showed beneficial effect of pulse electromagnetic field therapy (for 16 min twice daily) on fatigue in multiple sclerosis patients [28].

No adverse events were reported in our patients that were comparable with findings of most of the previous studies [7,27]. Short term use of magnet field therapy is usually well tolerated. The long term use of this treatment have not been evaluated.

In our study positive effect of magnet therapy was seen in the 4 week and continued for 8weeks. The evaluation time for the endpoints of the Lappin et Al studies was 4weeks [7].

The previous studies had somewhat varied outcomes, which could be due to the specific device, the study design, sample size (e.g.), treatment duration, type of MS.

Of course, there are statistical limitations in our study such as, no consideration of baseline level of patient's disability and no information about analgesics or treatments used by patients during the study period, Absence of any objective assessment method of the primary endpoint and small sample size in the placebo group because, more subjects may statistically demonstrate subtler effects.

7. Conclusion

According to our results pulsed magnetic therapy could alleviate paresthesia in MS patients .But trials with more patients and longer duration are mandatory to describe long-term effects.

Conflict of interest

The authors declares that there was no conflict of interest.

Funding

The work was not supported or funded by any drug company.

Acknowledgement

We thank Mansour Rezaei, Associate Professor, Department of Biostatistics & Epidemiology,

Kermanshah University of Medical Sciences, for comments that greatly improved the manuscript.

References

[1] F. Ashtari, V. Shaygannejad, Z. Farajzadegan, A. Amin, Does early-onset multiple sclerosis differ from adult-onset form in Iranian people, J. Res. Med. Sci. 15 (March (2)) (2010) 94–99.
[2] A.G. Beiske, E.D. Pedersen, B. Czujko, K.M. Myhr, Pain and sensory complaints in multiple sclerosis, J. Eur. Neurol. 11 (7) (2004) 479–482.
[3] H. Weber, K. Pfadenhauer, M. Stohr, A. Rosler, Central hyperacusis with phonophobia in multiple sclerosis, Mult. Scler. 8 (6) (2002) 505–509.
[4] W. -Pöllmann, W. Feneberg, Current management of pain associated with multiple sclerosis, CNS Drugs 22 (4) (2008) 291–324.
[5] V. -Yadav, L. Shinto, D. Bourdette, Complementary and alternative medicine for the treatment of multiple sclerosis, Expert Rev. Clin. Immnol. 6 (2010) 381–395.
[6] M.S. -Markov, Expanding use of pulsed electromagnetic field therapies, Electromagn. Biol. Med. 26 (3) (2007) 257–274.
[7] M.S. Lappin, F.W. Lawrie, T.L. Richards, et al., Effects of a pulsed electromagnetic therapy on multiple sclerosis fatigue and quality of life: a double blind, placebo controlled trial, Altern. Ther. Health Med. 9 (2003) 38–48.
[8] F. Bistoifi, Extremely low-frequency pulsed magnetic fields and multiple sclerosis: effects on neurotransmission alone or also immunomodulation? Building a working hypothesis, Neuroradiol. J. 20 (2007) 676–693.
[9] C.H. Polman, S.C. Reingold, G. Edan, M. Filippi, H.P. Hartung, L. Kappos, et al., Diagnostic criteria for multiple sclerosis: 2005 revisions to the McDonald criteria, Ann. Neurol. 58 (*2005*) 840–846.
[10] J.T. –Farrar, Young JPJr, L. LaMoreaux, et al., Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale, Pain 94 (2001) 149–158.
[11] G.A. Schumacker, G. Beebe, R.F. Kibler, L.T. Kurland, J.F. Kurtzke, F. McDowell, et al., Problems of experimental trials of therapy in multiple sclerosis: report by the panel on the evaluation of experimental trials of therapy in multiple sclerosis, Ann. N. Y. Acad. Sci. 122 (1965) 552–568.
[12] T.L.1 –Richards, M.S. Lappin, J. Acosta-Urquidi, G.H. Kraft, A.C. Heide, F.W. Lawrie, T.E. Merrill, G.B. Melton, C.A. Cunningham, Double-blind study of pulsing magnetic field effects on multiple sclerosis, J. Altern. Complement. Med. 3 (1) (1997) 21–29, spring.
[13] R. Sandyk, Treatment with weak electromagnetic fields improves fatigue associated with multiple sclerosis, Int. J. Neurosci. 84 (1996) 177–186.
[14] R. Sandyk, Application of weak electromagnetic fields facilitates sensory?motor integration in patients with multiple sclerosis, Int. J. Neurosci. 85 (1996) 101–110.
[15] R. Sandyk, Reversal of an acute parkinsonian syndrome associated with multiple sclerosis by application of weak electromagnetic fields, Int. J. Neurosci. 86 (1996) 33–45.
[16] R. Sandyk, Treatment with weak electromagnetic fields attenuates carbohydrate craving in a patient with multiple sclerosis, Int. J. Neurosci. 86 (1996) 67–77.
[17] R. Sandyk, Effect of weak electromagnetic fields on body image perception in patients with multiple sclerosis, Int. J. Neurosci. 86 (1996) 79–85.
[18] unlabelleda R. Sandyk, Suicidal behavior is attenuated in patients with multiple sclerosis by treatment with electromagnetic fields, Int. J. Neurosci. 87 (1996) 5–15, 14;
unlabelledb R. Sandyk, Treatment with electromagnetic field alters the clinical course of chronic progressive multiple sclerosis- a case report, Int. J. Neurosci. 88 (1996) 75–82.
[19] R. Sandyk, Lack of correlation between demyelinating plaques on MRI scan and clinical recovery in multiple sclerosis by treatment with electromagnetic fields, Int. J. Neurosci. 89 (1997) 29–38.
[20] R. Sandyk, Progressive cognitive improvement in multiple sclerosis from treatment with electromagnetic fields, Int. J. Neurosci. 89 (1997) 39–51.
[21] R. Sandyk, Immediate recovery of cognitive functions and resolution of fatigue by treatment with weak electromagnetic fields in a patient with multiple sclerosis, Int. J. Neurosci. 90 (1997) 59–74.
[22] R. Sandyk, Resolution of sleep paralysis by weak electromagnetic fields in a patient with multiple sclerosis, Int. J. Neurosci. 90 (1997) 145–157.
[23] R. Sandyk, Treatment with electromagnetic fields reverses the long-term clinical course of a patient with chronic progressive multiple sclerosis, Int. J. Neurosci. 90 (1997) 177–185.
[24] R. Sandyk, Treatment with electromagnetic fields improves dual-task performance (talking while walking) in multiple sclerosis, Int. J. Neurosci. 92 (1997) 95–102.
[25] R. Sandyk, Treatment with AC pulsed electromagnetic fields normalizes the latency of the visual evoked response in a multiple sclerosis patient with optic atrophy, Int. J. Neurosci. 93 (1998) 239–250.
[26] R. Sandyk, Yawning and stretching–a behavioral syndrome associated with transcranial application of electromagnetic fields in multiple sclerosis, Int. J. Neurosci. 95 (1998) 107–113.
[27] W. Brola, W. Wegrzyn, J. Czernicki, Effect of variable magnetic field on motor impairment and quality of life in patients with multiple sclerosis, Wlad Lek 55 (2002) l36–143 (Article in Polish).
[28] S. Mostert, J. Kesselring, Effect of pulsed magnetic field therapy on the level of fatigue in patients with multiple sclerosis: a randomized controlled trial, Mult. Scler. 11 (2005) 302–305.