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Effects of Para-Spinal Repetitive Magnetic Stimulation on Multiple Sclerosis Related Spasticity

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Abstract

Introduction: Spasticity is a major problem in multiple sclerosis (MS) patients directly affecting their quality of life. Despite having many treatment modalities, the clinical effectiveness of these modalities is at best modest.

Aim of the Study: The aim of this study was to test the effectiveness of repetitive peripheral magnetic stimulation (rpms) in decreasing spasticity and painful cramps in the lower extremities of MS patients. A secondary objective was to know whether this postulated improvement would result in an increase in the speed of walking of these patients.

Patients and Methods: Twenty six MS cases were randomly assigned either to 6 sessions of active 1 Hz rpms over the paravertebral region bilaterally (Group 1; n=18) or to sham stimulation (Group 2; n=8). Outcome measures included the Modified Ashworth Scale (MAS) for spasticity, self-reported spasm frequency and degree of pain associated with it, generalized body pains and 25 feet walking test. All measures were examined at baseline, after the end of treatment, and 2 and 4 weeks later. EDSS of all study patients did not exceed 6.5.

Results: There was no significant difference between the two studied groups at baseline. There was a significant difference between the two study groups in terms of muscle spasticity tested by MAS ($p= 0.05$), and spasm frequency and intensity ($p<0.0001$ for both). There was no significant difference between the two study groups in terms of duration taken to complete the 25 feet test or generalized body pain. There was no significant difference between relapsing remitting and secondary progressive MS cases receiving active stimulation.

Conclusions: Rpms helps ameliorating MS related spasticity and muscle spasms. Further studies are needed to look into the effects of this improvement on the quality of life and the activities of daily living of those patients.

Keywords: Multiple sclerosis; Peripheral repetitive magnetic stimulation

Introduction

Multiple sclerosis (MS) is the most common cause of physical disability in young adults [1].

More than two thirds of MS patients have moderate to severe spasticity that may present as muscle hypertonia or as sudden painful muscle cramps. There is a direct correlation between the severity of spasticity and the overall degree of disability and quality of life impairment [2].

Management of spasticity includes drug treatments [3], botulinum toxin injection for focal spasticity [4], and intrathecal baclofen [5]. Non pharmacological management is also considered, and this includes physical therapy [6], transcutaneous electric nerve stimulation [7], and non-invasive brain stimulation [8]. Surgery might be an option in refractory cases [9]. Despite the abundance of modalities available for the management of MS related spasticity, there is limited evidence to the efficacy of any of them [10].

Repetitive peripheral magnetic stimulation (rpms) over nerves, roots or muscle is gaining popularity as a safe and painless tool that may help in restoring motor control through activation of sensory proprioceptive fibers [11]. Several studies addressed the effect of rpms on decreasing spasticity and hence improving motor control. Most of these studies were open label, with variable targets of stimulation and outcome measures used [12-14].

The first study was done by Nielsen and colleagues in 1996. His group investigated the effect of 14 sessions of midline dorsal 25 Hz rpms in a group of MS patients. His patients demonstrated a decrease in muscle tone that reverted back to normal in one week [12]. Other studies used quasi-experimental or single case studies protocols. Different rpms stimulation parameters were used. Except for one study [13], only one stimulation session was delivered. All studies seemed to show a positive ill-sustained effect on spasticity and at times better motor control in cases with spinal cord injury due to MS or other disorders. (this paragraph was originally in the discussion section, we moved it to introduction as requested).

Aim of the Study

We hypothesized that rpms applied over the lumbar nerve roots would decrease muscle spasticity, pain frequency and intensity of cramps in a group of MS patients, and may hence improve their walking speed.

Methods

Thirty adult MS cases were recruited from the MS unit at Ain Shams university hospitals in the period between October 2012 and July 2013. MS diagnosis was made according to McDonald's criteria 2010 [15]. All types of MS were included in the study provided that their Expanded Disability Status Scale (EDSS) [16] score was less than or equal 6.5. They all had spasticity grade 1+, 2 or 3 according to modified Ashworth scale (MAS) [17], refractory to oral medications for at least 3 months. All patients were transcranial magnetic stimulation naive. Cases with fixed contractures were excluded as well as pregnant ladies, cases with implanted pacemakers or metallic devices. There was no change in medical treatment during the study period.

Patients were randomized using a computer generated sequence into an active treatment group (Group 1; n=20) who received 6 sessions of active 1 Hz rpms at a fixed intensity of 45% applied bilaterally at L2-4 spinal roots, 2 cm from midline. The sessions were received on alternate days over a period of two weeks, total of 6 sessions. Group 2 (Sham group; n=10) received the same protocol of treatment but the coil was placed at a right angle to the back muscles. Stimulation was done using a Dantec-Maglite magnetic stimulator with a figure of eight coil.

Follow up was done using MAS (that was calculated as half the sum of MAS on left and right knee), and 25 foot walking test [18] (participants were timed as they walked the 25 feet distance then turning and walking back the same distance) Both were done at baseline, after 2 weeks (on the same day of the last stimulation session), and two and four weeks later. According to 2009 revised EFNS guidelines, history and the use of diaries are among the most practical ways to follow up neuropathic pain [19]. Therefore, patients were instructed to keep track of their spasm frequency and intensity (how painful the spasm was) and to report their observations using a diary on a scale from 0-10. Patients were also instructed to report any other type of body pain that, to the best of their knowledge was not related to the site or the time of occurrence of a spasm. Participants were requested to report these symptoms starting one week before starting rpms and through the study period. All assessments, including the EDSS, were done by an independent neurologist in the MS unit who was blinded to the intervention given.

All patients completed the study except for two patients in the group 1 and two in group 2 who did not complete the follow ups

Statistical analysis

The collected data were statistically analyzed using SPSS statistical software (version 18). Descriptive statistics [mean and standard deviation] were used to assess the demographic data of the all patients. Oneway ANOVA and Chi square tests were used to compare both groups at baseline. Repeated measures ANOVA was used to compare between the different variables measured in the two groups across the four time points of the study.

The significance level was assumed at $p<0.05$ and high significance level at $p<0.01$.

Results

The sample included 17 females and 9 males. The mean age of the studied sample was 32.7 (±9.7). Twenty cases had Relapsing Remitting multiple sclerosis (RRMS) while 6 had secondary progressive multiple sclerosis (SPMS). The sample was randomly assigned to an active treatment group (A) and a sham control group (B). The characteristics of the study sample are illustrated in Table 1. There was no statistically significant difference between the two study groups at baseline.

Variable	Group A [n=18] [mean ± SD]	Group B [n=8] [mean ± SD]
Age	34.6 ± 9.2	32 ± 11.2
Gender [female/male]	14/4	4/4
MS type [RR/SP]	13/5	6/2
Duration of illness [years]	7.9 ± 5	5.8 ± 3.2
Number of attacks	5.8 ± 2.6	4.9 ± 2.4
EDSS	5.1 ± 1.2	5.2 ± 1.2
MAS	2 ± 0.5	1.7 ± 0.6
25 foot walking test duration in seconds	33.2 ± 36.6	40.8 ± 37.9
Pain intensity	4.4 ± 2.7	3.9 ± 3.4
Spasm frequency per day	3.7 ± 1.9	3.4 ± 1.7
Spasm intensity	5.8 ± 1.7	4.8 ± 1

Table 1: Demographics of the two treatment groups.

Regarding MAS, repeated measures ANOVA showed a significant difference between both treatment groups P=0.05, indicating that MAS improved in the active treatment group but not in controls (Figure 1).

EDSS: Expanded Disability status scale; MAS: Modified Ashworth Scale; MS; Multiple Sclerosis; RR: Relapsing Remitting; SP; Secondary Progressive

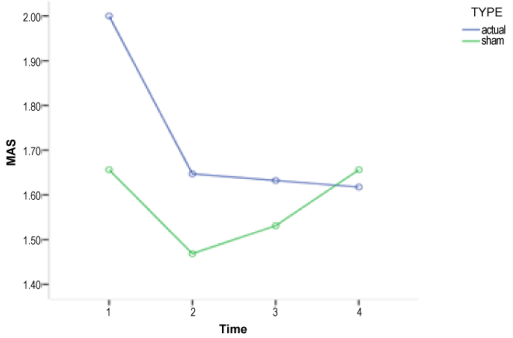

Figure 1: MAS in the two treatment groups across all time points. A persistent improvement in the active treatment group is clearly shown.

For spasm frequency and intensity, there was a statistically significant difference between active and sham treatment groups ($P<0.001$ for both parameters), indicating improvement in the active treatment group versus the control group (Figure 2). In terms of individuals who had other types of pain apart from muscle spasms

(n=16), there was no significant difference between the two study groups across all time points P=0.13.

Despite significant improvements in spasticity, spasm frequency and intensity in the active treatment group versus the control group, these changes were not reflected to a change in the time taken to complete the 25 feet walking test. There was no significant difference in time between the two study groups P= 0.45 (Figure 3).

Also there was no significant difference between RRMS and SPMS in the active treatment group in any of the outcome measures specified.

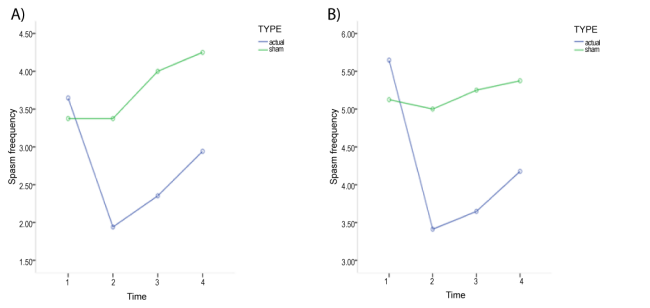

Figure 2: Spasm frequency (a. left), and intensity (b. right) across all time points. A persistent improvement in the active treatment group versus a transient improvement in the control group [placebo effect] that was rapidly reversed on stopping the sham TMS sessions.

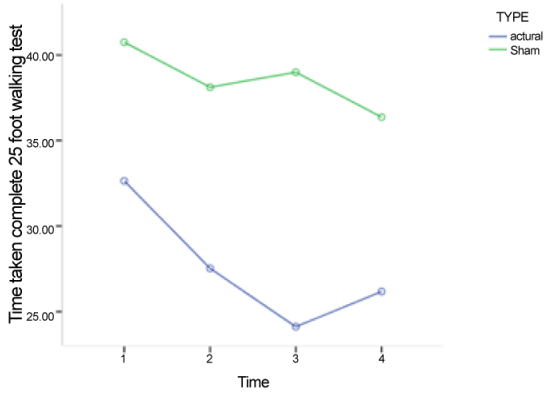

Figure 3: Time taken to complete the 25 foot test in the two treatment groups across all time points.

Discussion

Our study showed that repeated sessions of 1 Hz rpms applied over the nerve roots in the paravertebral region can decrease spasticity, spasm frequency and intensity in a sample of RRMS and SPMS cases with spinal cord lesions. This effect persisted for at least one month after the end of stimulation. To our knowledge, this is the second randomized double blind controlled study to be done investigating the role of rpms on nerve roots for spasticity in MS.

It was postulated that the positive effect of rpms is due to modulation of the activity of proprioceptive sensory afferents [13]. We may cautiously explain the similar clinical response seen to different stimulation parameters used by this effect. To prove this hypothesis, a recent functional MRI study showed that rpms increases brain activity in the posterior parietal cortex and the premotor cortex. Two areas known to be heavily connected and also known to have a major role in motor planning [11]. This may explain why rpms can enhance motor control.

We also looked into the effect of rpms on muscle spasms, a known disabling complication of marked spasticity and pain. Two types of pain were measured, pain associated with muscle spasms and other generalized body pains. It seemed logic that improvements in the baseline muscle tone testing by MAS, would be accompanied by improvements in spasm frequency and also a significant decrease in the pain associated with muscle spasms. This can again be attributed to central changes secondary to sensory afferent neuromodulation. Generalized body pains did not improve despite the fact the magnetic stimulation in general is well known for its antinociceptive effects. This can be attributed to many factors including the site of stimulation, the possibility of having pains in other body parts apart from the lower limbs, and the limited number of patients who had pains not related to spasticity at baseline evaluation (n=16).

There was no significant difference between the study groups regarding the time taken to walk 25 feet to and fro. This can be explained by the nature of the test with patients having to take a turn to complete it. This may mask the improvements in some patients who have coexisting neurological impairments as sensory or motor ataxia, and decreased visual acuity. Another probable explanation is that both groups had the chance to know their distances. Knowledge of performance or feedback is known to improve performance [20]. A third possibility is the wide standard deviation noticed due to recruitment of RRMS and SPMS cases. This may have reduced the power of the study to detect a change.

Limitations of Study

Small number of patients due to the need for repeated visits. It was difficult for MS patients to agree to come to hospital 6 times over 2 weeks.

Most of the assessment tests available and frequently used by most previous studies are relatively subjective.

There is no consensus on any neurophysiological tests that can be reliably used to evaluate the effect of rpms.

Conclusion

This study has shed some light on the role of rpms in the rehabilitation of MS patients with spasticity, a problem known to directly affect the quality of life of MS patients and with no clear evidence for the best management protocols. The active group showed significant improvement in terms of ameliorating spasticity and spasm frequency and intensity. A positive effect on walking speed was not detected. Further randomized controlled studies with more homogenous groups in terms of baseline gait speed, and further inspection of the effects of this technique on other aspects of ADLs is warranted.

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