The effect of combining low frequency repetitive trans-cranial magnetic stimulation and conventional rehabilitation in improving functional behavior of hemiplegic patients

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ABSTRACT

Purpose: Some new methods of treatment focus on using magnetic stimulation as a means of induction currents in the brain to produce therapeutic effects. The aim of this clinical trial was to determine the effects of repetitive transcranial magnetic stimulation (rTMS) plus routine rehabilitation on hand grip and wrist motor function in hemiplegic patients.
Materials and Methods: Twelve hemiplegic patients were assigned into the treatment group and received magnetic stimulation with routine rehabilitation program for 10 sessions, three times a week. Pre and post-treatment evaluations were done based on Barthel and Fugl-Meyer indexes and dynamometer.
Results: In the treatment group, significant improvement were observed in Barthel and Fugl-Meyer indexes and dynamometer (P = .010, P = .001 and P = .007, respectively).
Conclusion: Combination of rTMS with conventional treatment can improve hand muscle force and function in chronic hemiplegic patients.

Keywords: stroke; transcranialmagnetic stimulation; rehabilitation; motor skill; muscle force.

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INTRODUCTION

Stroke is the most common and debilitating neurological lesion among adults, and is a sudden onset of neurological signs because of brain blood supply impairment. After cardiovascular diseases and cancers, stroke is the third leading cause of death in the world. Stroke is responsible for more than 10-12% of all deaths. More than 50% of survivors catch long term disabilities.[1,2]

Brain stroke is considered as an upper motor neuron disease.[2] The patient's main problem is uncoordinated movement patterns associated with abnormal postural tone. Hemiplegia is a classic sign of cerebrovascular accident (CVA).[3] According to evidence, whenever CVA results in functional and neurological disorders, rehabilitation is effective and can improve functional ability. It has been noted that age cannot affect rehabilitation process outcomes. Focal neurological deficits resulting from stroke can reflect injury size and zone and collateral flow rate.[3]

In 1951, Twitchel provided a theory that still remains in force. He stated that after stroke, upper limb involves more than the lower limb and improvement in upper limb has more delay and less recovery. Post-stroke weakness intensity in the shoulder and restoration time of hand movements are two important characteristics for defining recovery level in upper limb.[4]

Functional movement therapy has been developed as a new approach in recent years. It is actually a combination of past approaches (Bruun Stroom, Kabat, Rood and Bobat) plus using functional movements in weight bearing or non-weight bearing patterns for increasing joint mobility and reducing hyper-tonicity in upper or lower extremities' muscles. The principles of this approach is obtaining full range of motion in all joints by using complex functional patterns and joint mobility, plus eliminating muscle imbalance by using stretch and strengthening, and motor control restoration of affected limb.[5]

Repetitive transcranial magnetic stimulation (rTMS) is a novel technique that is widely used in treatment of depression, mania, schizophrenia, Parkinson, epilepsy and chronic pain. In recent years rTMS is used in post-stroke care.[6] While recent advances in stroke care have primarily been concentrated on the neuro-protective and neurovascular fronts, tools used to study and alter cortical function have had a significant role in all parts of post-stroke care: diagnostic, prognostic, and interventional.[7]

Depending on the type of stimulation, transcranial magnetic stimulation (TMS) can affect nervous system in two ways: single or paired pulse. TMS causes neurons to depolarize and discharge an action potential in the brain cortex beneath the stimulating area.[8] Long-lasting effects of TMS appear by using rTMS. Depending on the intensity of stimulation, coil orientation and frequency; rTMS can change the excitability of the corticospinal tract. Although the mechanism is not clear now but it is widely believed that rTMS can reflect changes in synaptic efficacy akin to long-term potentiation and long-term depression.[9] Safety, ethical considerations, and application guidelines for the use of TMS have been approved by Rossi and colleagues.[10]

Regarding major rehabilitation, hemiplegic treatments are focused on lower extremities. Since upper extremity disabilities are common and persistent, using newer treatments seem to be necessary. Different routine rehabilitation methods are used to improve function in hemiplegic patients. Based on their results, addition of new treatments for chronic stage is recommended because of less effectiveness of traditional approaches. Several investigations have been performed to study the effect of rTMS on motor function and grip strength of upper limb in hemiplegic patients.[11-19] These investigations have used different frequencies and treatment sessions, and/or present motor function and grip strength solely. However, to the researcher's knowledge, measuring both variables in one study using highly safe frequencies (1 Hz) of rTMS in combination with routine rehabilitation has not yet been done.[17,19-23]

This study set out to determine the effects of rTMS plus routine rehabilitation on hand grip and wrist motor function of hemiplegic patients.

MATERIALS AND METHODS

Subjects

The study protocol was reviewed and approved by the Ethics Committee of the Tarbiat Modares University (Tehran) and performed in a medical center in Tehran, Iran. According to previous studies and in order to achieve 80% chance ($\beta = 0.20$) of detecting 20% difference ($\alpha = 0.05$) in improvement among treatment group, treatment group should have included at least 12 participants. In this clinical trial study, 12 volunteers that were examined by a physician for having the inclusion criteria were assigned to the treatment group.

The inclusion criteria included hemiplegia in the dominant side after a single stroke, middle cerebral artery involvement, spasticity due to stroke, being more than two months past their stroke, and both sexes of ages 30 to 65 years old. Exclusion criteria included stroke due to cardiac embolism, permanent injuries of upper extremities, e.g. fractures, neurologic disorders, e.g. Parkinsonism, multiple sclerosis (MS), etc., upper extremity mobility restriction due to any other reason, epilepsy or history of epilepsy in family, intracranial implantation or clips, pacemaker, lesion in occipital, limbic system and complementary area, and not being able to cooperation for 4 weeks.

Data Collection

Firstly, the participants were informed regarding the procedure and the aim of the study and informed consent was obtain from them. Demographics and some other characteristics of every participant (such as: sex, age, weight, height, job, history of stroke, motor disabilities according to the subject opinion, previous physical therapy management, etc.) were collected by an administered questionnaire.

Balance, sensation, pain and joint range of motion were measured for motor recovery based on Bruun Stroom's approach by Fugl-Meyer's questionnaire. Reliability and validity of this scale for assessment of the upper extremity and lower extremity motor function and as an stroke severity stratification variable across different stroke recovery time points has been established previously.[24,25] Recently, Sullivan and colleagues[26] have shown that intra-rater reliability for the expert rater was high for the motor and sensory scores (range 0.95–1.0). Inter-rater agreement between expert and therapist raters was high for the motor cores (total of 0.98; upper extremity, 0.99; lower extremity, 0.91) and sensory scores (total of 0.93; light touch, 0.87; proprioception, 0.96). Assessment of motor function of upper extremity was performed in 33 tasks and each task was scored from zero (complete disability) to two (full, coordinate and normal performance).

Martin vigorimeter was used to measure grip strength. The maximum value on three trials with each patient was recorded and considered as grip strength. Molenaarand colleagueas[27]demonstrated that the intraclass correlation coefficient for the Martin vigorimeter was 0.84 [95% confidence interval (CI): 0.77 - 0.89] for the dominant hand and 0.86 (95% CI: 0.80 - 0.90) for the non-dominant hand.

The reliability of Bartel index has been proven in post-CVA patients[28,29] and it used to measure functional assessment of the participants. The index is an ordinal scale including ten daily life activities. The original Bartel index was scored in steps of five points to give a maximum total score of 100.[30]

One day before starting training sessions and one day after the final session, all subjects were tested by the same physical therapist and in the same condition.

Interventions

The treatment group had the rTMS treatment which was followed by conventional treatment. rTMS system was set on 1 Hz frequency, 20 minutes duration, 60-80% of motor threshold, continuous current and intensity of 1.5-2 Tesla on coil surface. rTMS was done with a 100-mm figure-8 coil. The coil was placed tangentially over the contralesional M1 at the optimal site for the first dorsal interosseous (FDI) muscle. The optimal site was defined as the location where stimulation of slightly supra-threshold intensity elicited the largest motor evoked potential in the FDI. Electromyographic activity was recorded from silver-silver-chloride electrodes positioned in a belly-tendon montage on the skin overlying the FDI, and the signal was amplified, filtered (50 to 2000 Hz) and digitized at a sampling rate of 5000 Hz for off-line analysis (Neuropack; Nihon Koden).[31]Afterwards, the current increased until the FDI muscle showed minimal contraction. This was considered as a patient's motor threshold.

Then the participants received routine rehabilitation program for the upper extremity. After 10 minutes of Faradic electrical stimulation for wrist and finger extensor muscles, the participants exercised functional movements for 30 minutes in the same predetermined program. Rehabilitation program included: upper extremity functional patterns, elbow, wrist and fingers mobility, gentle stretch of hypertonic muscles, strengthening of weak muscles in weight bearing and non-weight bearing patterns, muscle imbalance elimination, motor control restoration of involved extremity, reduction of muscle stiffness and range of motion restoration. This procedure was performed in 10 sessions totally, three 60-minute sessions per week.

Statistical Analysis

Descriptive statistics were used for the participants' characteristics. The One-Sample Kolmogorov-Smirnov Test procedure was used to observe the data distribution. Student's *t*-tests were performed to find statistically significant difference between mean value of each variable in pre-tests and post-tests results. Confidence interval was considered to be at 95% (P >.05). Data analysis was conducted by the statistical package for the social science (SPSS Inc, Chicago, Illinois, USA) version 19.

RESULTS

Twelve hemiplegic patients were assigned into the treatment group and received magnetic stimulation with routine rehabilitation program for 10 sessions, three times a week. The inclusion criteria included hemiplegia in the dominant side after a single stroke, middle cerebral artery involvement, spasticity due to stroke, being more than two months past their stroke, and being between 30 to 65 years old. Some of the exclusion criteria included stroke due to cardiac embolism, neurologic disorders, epilepsy, intracranial implantation or clips. Pre and post-treatment evaluations were done based on Barthel and Fugl-Meyer indexes and dynamometer.

The mean age of patients was 55.17 ± 5.42 years old. The mean height and weight in patients were 171.83 ± 0.90 cm and 84.50 ± 10.86 Kg. The mean BMI of patients was 28.53 ± 1.86 and duration between stroke and study participation was 24.00 ± 8.29 months.

In the treatment group, the mean score of Fugl-Meyer questionnaire significantly increased after treatment by rTMS (P < .001). When compared with pre-treatment, mean score of Barthel Index questionnaire had also significantly increased (P = .01). Mean value of grip strength showed statistically significant increase in post-test measure in comparison with pre-test measure (P = .001) (Table 1).

No adverse side-effects were reported during or after the course of the study with safe frequency of rTMS. Statistical analysis of Fugl-Meyer, Bartel index and Martin vigorimeter measures after 10 sessions showed significant improvements for all variables in the treatment group.

Table 1. Comparison of variable measures between two times of measurement in the treatment group.

Variables	Pre-test	Post-test	*P*-Value
Fugl-Meyer Index (Score)	19 ± 2.45*	26.5 ± 2.88*	.001
Bartel index (Score)	68.33 ± 14.02	78.33 ± 14.02	.01
Vigorimeter measures (Kib)	6.83 ± 4.88	10.5 ± 4.93	.001

key: Kib, Kilopound , * Mean ± SD.

DISCUSSION

In this study it was demonstrated that rTMS plus routine rehabilitation in post-stroke patients, can result in functional gains in motor function. Several studies have shown that rTMS can result in grip strength in post-stroke patients.[11-14,21,32] Improvements in Bartel index and grip strength measures in the experimental group of this study are consistent with Khedrand colleagues,[33] showing that 10 consecutive days of rTMS employed as an add-on intervention to normal physical and drug therapies can improve immediate clinical outcome in early stroke patients. Furthermore, improvement in Fugl-Meyer measures in the experimental group is consistent with several other reports.[15,16,18]

Khedr and colleagues[22] have shown that, 1 Hz rTMS applied over M1 of the unaffected hemisphere significantly increases motor cortex excitability of the affected hemisphere and decreases cortical excitability of the unaffected hemisphere. Another possible mechanism of rTMS for achievement of motor function recovery may be facilitating practice-dependent plasticity and improving the motor learning performance in post-stroke patients.[11] Gershon and colleagues[34] have reported that rTMS can reduce depression. Laboratory findings in rats have shown that transcranial magnetic field stimulation induces neurogenesis of the subventricular zone.[35] These may be two possible mechanisms that can result in functional improvements in patients.

Thus, it is possible that improvement of hemisphere balance excitability with rTMS and increasing the brain output to upper limb, followed by exercise therapy, can improve the functional ability of the affected hand. Increase in muscle activity improves functional outcomes in daily functions such as wearing clothes, closing buttons, going to toilet, etc. which means better questionnaires score.

For gaining more functional recovery in post stroke patients, some of authors suggest that longer duration of rehabilitation and more intensity of training are needed and patients should be in acute or sub-acute phase.[36,37,38] It is likely that rTMS can reduce time and session of treatments in chronic stroke patients.

Since grip strength has been shown to be a predictor of disability and mortality in older adults, remediation of low grip strength should be an important aspect of treatment for individuals with stroke.[39] However, larger prospective studies are needed to confirm our findings of advantages of rTMS in functional mobility of stroke patients.

CONCLUSION

The main finding of this study is that rTMS plus routine rehabilitation can increase grip strength and functional ability. Thus, it seems that using rTMS plus routine rehabilitation program for post-stroke patients can accelerate restoration of function and decrease their disability in less time duration. For discovering the intracranial changes, intracranial assessment equipment such as functional MRI and motor evoked potentials must be used in future studies. Longer follow-up are proposed for future researches. Also, it is suggested that the results of this safe treatment (1 Hz frequency tTMS plus conventional therapy) be compared with treatment with high frequency rTMS plus conventional therapy for establishing better treatment methods.

CONFLICT OF INTEREST

None declared.

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