EFFECT OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION ON PATIENTS WITH LUMBAR RADICULOPATHY

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ABSTRACT

Background: Lumbosacral radiculopathy is a pain condition that occurs when nerve roots in the lower back are compressed or irritated. Depending on which nerve root(s) are affected, patients may experience a range of symptoms that impact the corresponding dermatome or myotome. ***Objective:*** To determine the efficacy of repetitive transcranial magnetic stimulation in improving pain of unilateral lumbar radiculopathy. ***Subjects and Methods:*** fifty-three patients of both sexes were recruited from the outpatient clinic of Ain Shams Hospital, Ain Shams University, Egypt. Their ages ranged from 20 to 45 years. Patients suffered from persistent unilateral pain in the sciatic nerve distribution. Patients had been assigned into two groups. rTMS (repetitive Transcranial Magnetic Stimulation) group included 28 patients, 20 patients (active rTMS) received real rTMS and 8 patients (control rTMS) received sham rTMS. All techniques were combined with conventional physical therapy program of discogenic back pain management. The two groups were assessed by the two assessment scales (Visual Analogue Scale and Oswestry Low Back Pain Disability Questionnaire) and the goniometer for hip and trunk flexion before, intermediate (after 2 weeks), and after treatment (after 4 weeks). Hospital Anxiety and Depression Scale was conducted before treatment just to exclude patients who had pain due to depression. Each patient in both Groups received 6 sessions of rTMS (real or sham) every other day, the duration of each session was 20 minutes, in addition to 12 sessions of the conventional physical therapy program were performed every other day for 4 weeks. ***Results:*** The statistical analysis of (rTMS Group) revealed that there weren't any significant differences between pre and post-treatment for all study variables (VAS, hip flexion ROM, trunk flexion ROM, and ODQ), as well as the sham group. This indicating that there is no statistical significant differences between pre and post treatment which revealed that rTMS combined with traditional physical therapy has no statistical effect on pain due to lumber radiculopathy. ***Conclusion***: rTMS, hasn't any statistically effect on reliving pain due to lumber radiculopathy.

***Key Words*:** Repetitive Transcranial Magnetic Stimulation (rTMS) - Lumbar radiculopathy.

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1. INTRODUCTION

Subjects can experience a predictable constellation of symptoms caused by cycles affecting one or more of their lumbosacral nerve roots, which can cause varying degrees of discomfort, numbness/tingling, weakness, and problems with their gait. Depending on which nerve root is damaged, patients can experience symptoms in specific dermatomes or myotomes. **(Alexander & Varacallo 2020).**

The most common cause of lumbosacral radiculopathy is a herniated disc impinging on or irritating a nerve root. L4-L5 and L5-S1 are the most commonly impacted intervertebral discs, which result in lumbosacral radiculopathy in cases of posterolateral disc protrusion, also known as sciatica. Most patients describe the clinical presentation of lumbosacral radiculopathy as acute, dull, piercing, throbbing, stabbing, shooting, or scorching pain and paresthesia in the affected dermatome ***(Takla 2019)***.

A wide range of pathological pain conditions, such as fibromyalgia, chronic post-stroke pain, and complex regional pain syndrome, have all been treated with brain stimulation techniques. Pain relief is evident from preliminary clinical studies of both invasive and non-invasive procedures. Various types of noninvasive and invasive brain stimulation are currently being used in clinical settings to treat chronic pain ***(O'Connell et al., 2014).***

Non-surgical stimulation treatments are a more convenient and safer alternative to invasive procedures. Repetitive transcranial magnetic stimulation (rTMS) is a method that stimulates the outer layer of the brain, known as the cerebral

cortex, by utilizing a stimulating coil positioned on the scalp. Alterations in magnetic fields result in the direct induction of electric currents within neurons, specifically brain cells. To bring about modifications in brain activity, these sequences of stimuli are administered to the target cortex region, influencing both nearby and remote brain regions ***(Leo & Latif 2007).***

Exercise therapy is commonly employed to alleviate chronic low back pain. Multiple additional systematic reviews have discovered that exercise has the potential to assist individuals suffering from enduring low back pain. In some instances, it seems that exercise therapy alone is not enough to fully alleviate chronic lower back pain. It is necessary to combine exercise with other forms of medication and non-medication treatments. As a result, there have been suggestions for implementing new approaches within a comprehensive program involving multiple disciplines **(Hayden et al 2005).**

Low back pain is a highly common musculoskeletal condition observed in clinical practice. It holds the unfortunate distinction of being the leading cause of disability in developed nations, resulting in significant financial burden on the healthcare system annually. Epidemiological studies have shown that the occurrence of low back pain varies from 5% to over 30%, with a lifetime occurrence rate of 60% to 90%. The range of potential causes for low back pain is extensive, and should encompass the consideration of lumbosacral radiculopathy as well as other related conditions ***(Alexander & Varacallo 2022).***

Untreated chronic radicular pain poses challenges in management due to its potential to induce long-lasting anatomical and metabolic alterations in the spinal cord and thalamus. Consequently, these changes can become more centralized and permanent over time ***(Haleem & Sohal 2017)***.

Previous studies on non-surgical interventions for lumbosacral radiculopathy have discovered factors that may indicate unsuccessful treatment, such as the need for subsequent surgery, ongoing pain, disability, or a perceived lack of recovery. Therefore, it is crucial to explore alternative approaches for non-invasive procedures ***(Suri et al. 2015).***

Noninvasive brain stimulation procedures such as repetitive transcranial magnetic stimulation (rTMS) have shown promise in the treatment of many types of chronic pain.

SUBJECTS & METHODS

1.1. Study design

The design of the study was a randomized controlled trial (RCT). Sealed envelopes were prepared in advance and the different methods of study intervention which are active rTMS and sham rTMS were written and put inside a box. All interventions were combined with conventional physical therapy program. Randomization was performed prior to the start of the pretest by a subject who was not involved in the assessment or treatments.

1.2. Procedures:

Preparation of patients and subjects:

All patients were diagnosed by MRI and referred by a physician. They were asked to fill the informed consent. Each patient was informed about the procedure of the study protocol. Also they underwent neurological assessment by the neurological assessment sheet. Sensory and motor assessment for L4, L5 and S1 roots and reflex assessment 'ankle reflex" were done to exclude patients with motor dysfunction and upper motor neuron lesions. Straight leg raising test was done for all patients as a Special test to confirm the diagnosis of sciatica.

Assessment tools

Were performed pre, by the end of last NIBS session (after 2 weeks) and post treatment (4 weeks).

1. ***Visual analogue scale (VAS): -***

A visual analogue scale (VAS) consists of a linear line that is typically 10 cm long, running horizontally. It is accompanied by two descriptive statements at each end. The scale is commonly labeled from 0 (left, indicating the least extreme) to 10 (right, indicating the most extreme) ***(Yeung et al., 2019).***

Patients were instructed to assess their discomfort level by connecting a line between two contrasting statements. The scale was then scored by measuring the distance from the minimum endpoint to the marked position at a predetermined interval.

2. ***Universal goniometer: -***

A universal goniometer is a tool used for measuring angles or facilitating rotation of an object to a specific position. It consists of three components: the body, the fulcrum, and the stationary arm. This device is commonly utilized for assessing the range of motion (ROM) of hip flexion during straight leg raising and trunk flexion from a standing position.

3. ***Oswestry Low Back Pain Disability Questionnaire:***

This tool is utilized to evaluate a patient's long-term functional limitations. It is widely recognized as the benchmark for assessing functional outcomes in individuals with low back issues. The scoring system ranges from 0% to 20%, 21% to 40% indicating moderate disability, 41% to 60% representing severe disability, 61% to 80% indicating being crippled, and 81% to 100% representing being bed-bound ***(Fairbank & Pynsent 2000).***

Patients were required to select a single option in each category that most accurately corresponded to their specific issue as described by each statement.

Hospital Anxiety and Depression Scale (HADS):
This measure was created to rule out the possibility that the discomfort was caused by depression. (HADS) Includes 14 items to provide anxiety and sadness ratings ranging from 0 to 7. Normal, 8-10 denotes borderline abnormal (borderline case), while 11-21 implies severe abnormality. Unusual (case) ***(Snaith 2003).***
Patients were advised to select responses based on symptoms they had encountered in the preceding week and were requested to provide spontaneous answers without excessive contemplation.

1.1. Intervention:
Seventy patients from both sexes suffering from lumber disc lesion (L4, L5 – L5, S1) with unilateral sciatic pain were assessed for eligibility for the study, sixty four patients met the inclusion criteria while six patients didn't meet the inclusion criteria and were excluded. Eleven patients did not complete the study, some of them were living far away from the hospital and they would not be able to attend the sessions, corona virus pandemic diseases limitations to continue sessions and others left without clear reasons. They were assigned into two groups; rTMS (repetitive Transcranial Magnetic Stimulation) group included 28 patients, 20 patients (active rTMS) received real rTMS and 8 patients (control rTMS) received sham rTMS. Each patient received six sessions of real or sham rTMS every other day, the duration of each session was twenty minutes. The treatment was applied for two weeks. Two groups received conventional physical therapy program of discogenic back pain management every other day for four weeks (twelve sessions). There allocation is represented in the flow chart **(figure 3)**

Transcranial magnetic stimulation (Fig 1):-
Apparatus: - MagVenture Magpro X 100 with stimulator dynamic liquid cooled film coil (figure of eight, diameter 17cm) (Denmark).
Application: - Patients were seated in a cozy reclining chair and instructed to maintain a relaxed hand position. The resting motor threshold was determined in the abductor policis brevis muscle using the technique outlined by ***(Rossini et al., 1994).*** Repetitive magnetic stimulation was administered by employing a figure-of-eight coil positioned at a 45^{o} angle to the inter hemispheric fissure, with the handle directed towards the back. The intervention involved the application of either real or sham rTMS to the contralateral (M1) region, opposite to the side experiencing pain. The treatment was delivered in a series of 20 sets, each lasting 6 seconds, with a 54-second break between sets. The intensity was set at 90% of the motor threshold, and the stimulation rate was maintained at 10 Hz (equivalent to 1200 pulses) for a total duration of 20 minutes per day ***(Malavera et al., 2016).***

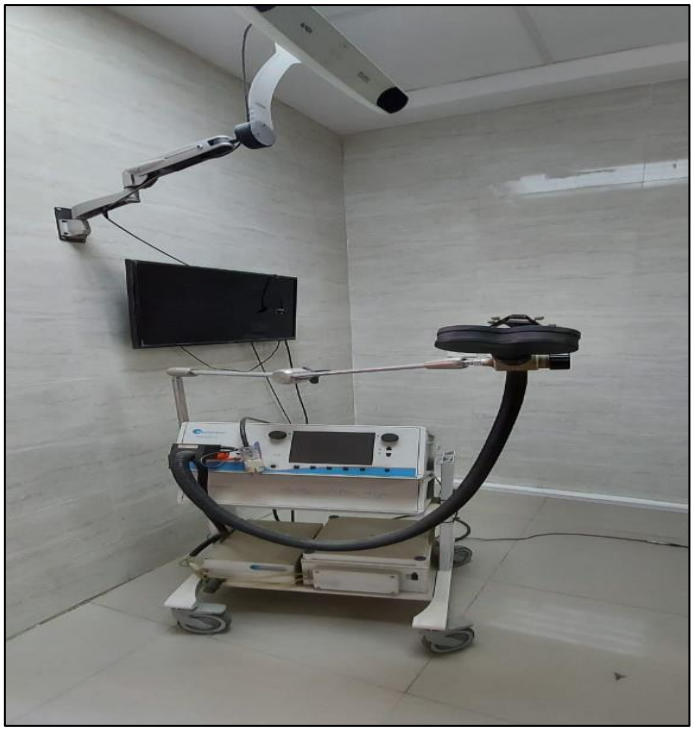

Figure 1. MagVenture Magpro X 100. transcranial magnetic stimulation device.

Transcranial direct current stimulation (Fig):-

Apparatus:- 4X1 High Definition - Transcranial Direct

Current Stimulation Multichannel Stimulation Interface Model 4X1-C3A (USA).

Application:- The experiment included either active or sham tDCS intervention. Participants were comfortably seated in a reclining chair. The anode was strategically positioned over either C3 or C4 to specifically target M1 on the side of the body that was not in pain. As for the cathode, it was placed over the chin. A constant current with an intensity of 2 mA was administered for a duration of 20 minutes. ***(Ngernyam et al.,2015).***

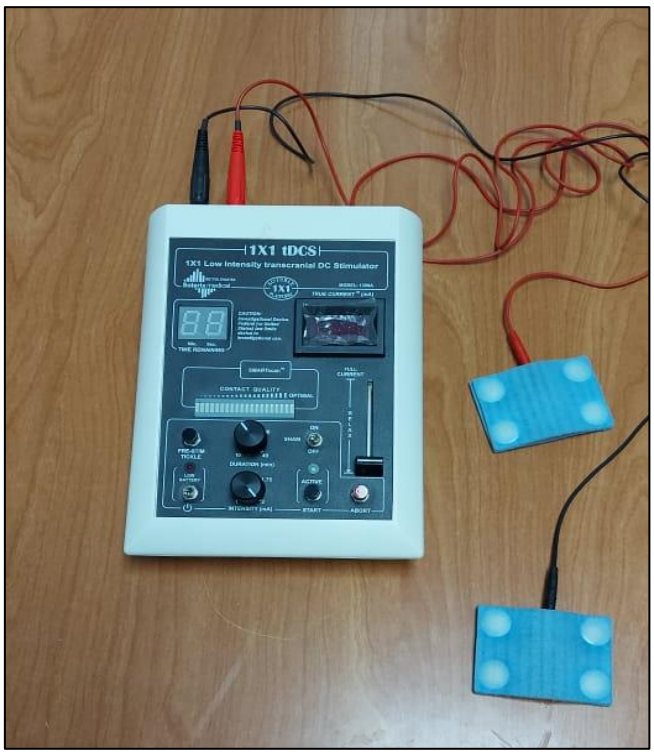

Figure 2. 4X1 High Definition - Transcranial Direct Current Stimulation Multichannel Stimulation Interface Model 4X1-C3A (USA).

Conventional physical therapy program:-

Exercises program (Michell 2014):-

Back exercises with 10 repetition of each in the form of:-

Prone on elbows; Patients were propping themselves up on their elbows while their lower body was supported by the plinth. It was important for their body to form a straight line from the back of their head to their heels. They were instructed to gradually lower their chest towards the floor and subsequently push back up.

Prone on hands; Patients began by positioning their bodies with their hands supporting them, placed shoulder-width apart. They were instructed to gradually lower their chests towards the floor by bending their arms. Then, they were prompted to push back up by straightening their arms. Finally, they advanced to extending their backs with their hands positioned behind them.

Bridging exercises with 10 repetitions in the form of:-Patients started in supine position, arms either side to hips, palm facing down, shoulders away from ears. Knees should be bent, heels as close to bottom as is possible. Spine should be neutral, with a slight curve, allowing for a small gap under lower back. Patients were asked to Breathe in then Breathe out, belly moves towards spine to engage abdominals and tailbone lengthens towards heels. Press through the hands and feet at the same time, lifting the tailbone and hips. Lower the middle and lower spine towards the ceiling to create a straight line between the shoulders and hips. Finally, release the back onto the plinth.

Quadriped exercises with 10 repetitions of each lower limb in the form of:- Patients assume the position commonly known as "cat position" by getting on all fours. They should place their hands shoulder-width apart, with their fingers pointing forwards and their shoulders relaxed away from their ears. Their knees should be hip-width apart. It is important for patients to maintain a neutral position in their spine. They should be instructed to extend their right leg back while pointing their toes away. To ensure proper alignment of the spine, patients should keep their gaze down towards the plinth. It is crucial for the hips to stay centered and avoid tipping to the left or right. The same sequence should be repeated for the left side.

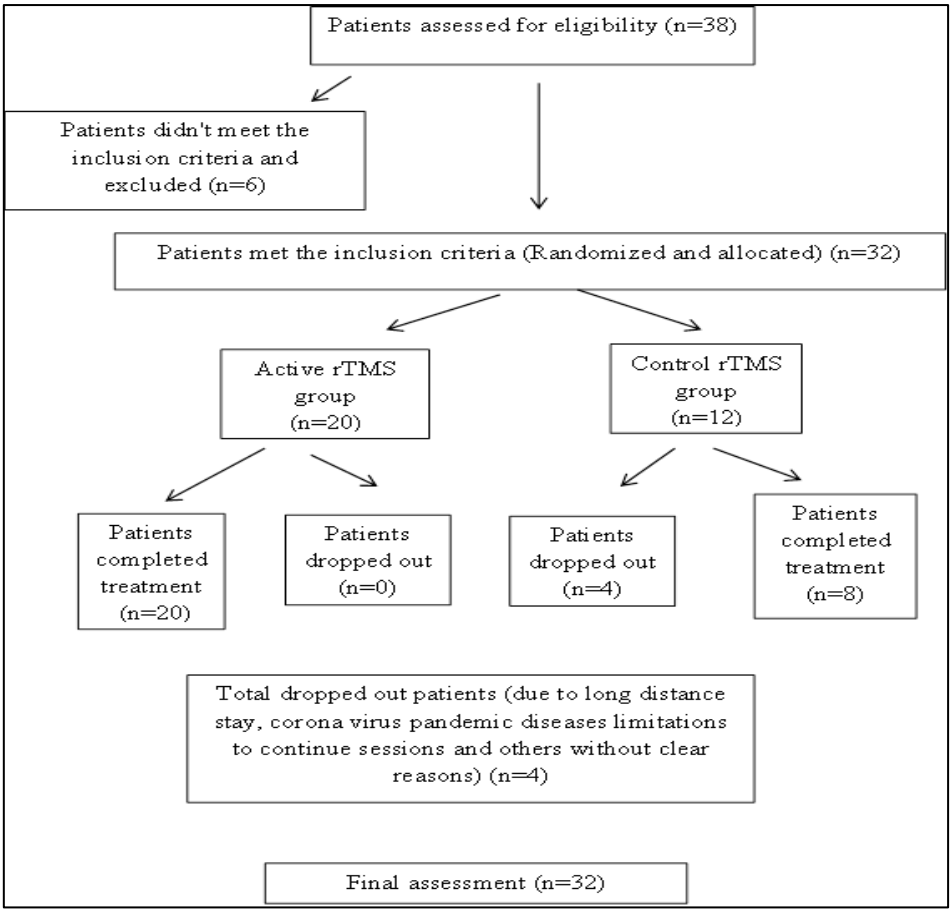

Figure 3. Flow chart of study participant

STATISTICAL ANALYSIS

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:

The data for age includes quantitative descriptive statistics such as the mean and standard deviation.

The data for gender and side of radiculopathy includes qualitative descriptive statistics such as the number and percentage.

For group comparisons, the Mann-Whitney U test, median, and interquartile range were used. This includes assessing the differences at the assessment points for all assessment parameters.

In terms of statistical significance, all analyses were considered significant if the probability level (P) was less than 0.05.

RESULTS

Data collection

The current study was done to test the efficacy of repetitive transcranial magnetic stimulation on patients with lumbar radiculopathy. Patients had been assigned into two groups: rTMS groups including active (20 patients) and control (8 patients). Total dropped out patients were (11 patients) (due to long distance stay, corona virus pandemic and others without clear reasons).

I- Demographic data:-

General description of the recruited subjects (Tables 1,2,3):

The median age of the whole group was 40 and the range was from 20 to 45. Male patients constituted 30.19% and females 69.81%.

On comparing the active and control groups of TMS, we found non-significant differences regarding age, gender and side of radiculopathy.

Table 1. Comparison of general characteristics among groups:

	TMS Active (no.=20)		TMS Control (no.=8)		Mann- Whitney U test	
	median	IQR	median	IQR	Z	p
Age	40.00	9	40.50	15	-0.26	0.80
Gender (*female*)^	17	85.0%	4	50%	3.733	0.053
Side of radiculopathy (*right*)	10	50%	4	50%	0	1

Comparisons among 4 assessment points within each group

A) Visual Analogue Scale (VAS)

Showed non-significant differences between active and control groups across different assessment points **(Table 2).**

Table 2. Comparisons among 3 assessment points in TMS group in VAS

Visual Analogue Scale (VAS)	TMS Active (no.=20)		TMS Control (no.=8)		Mann- Whitney U test	
	median	IQR	median	IQR	Z	p
Baseline	9.00	1.75	8.00	3.00	-1.346	0.178
Δ- Baseline- After 6 sessions	3.00	2.00	2.50	3.50	-0.909	0.363
Δ- After 6 sessions -After 1 month	0.00	1.00	0.00	0.00	-1.231	0.218

B) Goniometer Hip Flexion:-

Showed non-significant differences between active and control groups across different assessment points **(Table 3).**

Table 3. Comparisons among 3 assessment points in TMS group in Goniometer Hip Flexion

Goniometer Hip Flexion	TMS Active (no.=20)		TMS Control (no.=8)		Mann- Whitney U test	
	median	IQR	median	IQR	Z	p
Baseline	128.50	20.00	128.50	31.25	-0.561	0.575
Δ- Baseline- After 6 sessions	15.00	16.25	8.00	15.75	-1.634	0.102
Δ- After 6 sessions -After 1 month	0.00	0.00	0.50	7.75	-.322	0.748

C) **Goniometer Trunk Flexion:-**

Showed non-significant differences between active and control groups across different assessment points **(Table 4)**

Table 4. Comparisons among 4 assessment points in TMS group in Goniometer Trunk Flexion

Goniometer Trunk Flexion	TMS Active (no.=20)		TMS Control (no.=8)		Mann- Whitney U test	
	median	IQR	median	IQR	z	p
Baseline	90.00	8.50	102.50	21.50	-1.901	0.057
Δ- Baseline- After 6 sessions	10.00	5.25	13.50	15.25	-1.489	0.136
Δ- After 6 sessions -After 1 month	0.00	6.50	0.00	8.25	-.313	0.754

D) **Oswestry Low Back Pain Disability Questionnaire**

Showed non-significant differences between active and control groups across different assessment points **(Table 5).**

Table 5. Comparisons among 4 assessment points in TMS group in Oswestry Low Back Pain Disability Questionnaire

Oswestry Low Back Pain Disability Questionnaire	TMS Active (no.=20)		TMS Control (no.=8)		Mann- Whitney U test	
	median	IQR	median	IQR	z	p
Baseline	48.90	12.28	35.55	20.55	-1.581	0.114
Δ- Baseline- After 6 sessions	11.15	15.59	5.55	6.13	-1.581	0.114
Δ- After 6 sessions -After 1 month	0.00	1.65	0.00	1.65	-0.430	0.667

DISCUSSION

The current study was conducted to test the efficacy of repetitive transcranial magnetic stimulation combined by the traditional physical therapy program on patients with lumbar radiculopathy. The results showed that rTMS combined by traditional physical therapy program hasn't statistically significant effect in relieving lumber radicular pain.

The findings of this study are in accordance with the research conducted by **Hosomi et al.** Their study encompassed a multicenter, randomized,

sham-controlled trial aimed at assessing the efficacy of repetitive transcranial magnetic stimulation (rTMS) on the primary motor cortex (M1) in individuals suffering from neuropathic pain (NP). The study involved individuals with various forms of neuropathic pain who were randomly divided into two groups. One group received active repetitive transcranial magnetic stimulation (rTMS) on the primary motor cortex (M1), specifically targeting the area of the body that caused the most discomfort. The other group received sham rTMS. The results showed that rTMS did not offer immediate pain relief for the entire group of participants in the study **(Hosomi et al., 2020).**

Another research that confirms the conclusions of this study is conducted by **Mori et al.,** who examined the pain-relieving effects of repetitive transcranial magnetic stimulation (rTMS) on the motor cortex (M1) using a figure-of-8 coil applied to various pain locations. The outcomes indicated that rTMS was effective in alleviating neuropathic pain (NP) in the upper limb, but not for NP in the face or lower limbs **(Mori et al.,2021).**

The current study's results were supported by the research conducted by **Hosomi et al.** and **Mori et al.,** which found that using a figure of eight coil for rTMS stimulation on M1 did not effectively reduce pain in the lower limb. 1)These researchers suggested that the positive outcomes observed in the placebo group could be attributed to a placebo effect, as well as other factors like the psychological and social benefits of participating in a trial. 2) The M1 foot region, situated in the deep recesses of the brain, poses a challenge for effective stimulation, resulting in weaker pain-relieving outcomes compared to the M1 hand region. 3) Achieving sufficient stimulation in the deep brain region, specifically the M1 foot area, proves to be a challenging task with the figure-of-8 coil. In contrast, the H-coil and double-cone coil demonstrate superior efficacy in alleviating pain. **(Hosomi et al., 2020)** and **(Mori et al.,2021)**.

The findings of the present study contradicted the results of **Hosomi et al.,** who conducted a crossover trial RCT on 70 patients with (NP) recruited from seven Japanese centers. In their study, they administered 10 stimulation sessions of 5 hz rTMS and conducted follow-up examinations at least 17 days later. After undergoing 5Hz rTMS sessions over the M1, patients experienced notable improvement in their scores on a visual analogue scale (VAS) and the short form of the McGill pain questionnaire in the short term. This improvement was significantly greater compared to the results of sham sessions. The study findings indicate that daily high-frequency rTMS of M1 is well-tolerated and offers temporary relief from pain in patients with NP **(Hosomi et al. 2013).**

Contrary to the findings of the present study, **Lefaucheur et al.** demonstrated that delivering rTMS at a frequency of 10 Hz over M1 can alleviate neuropathic pain, whereas a frequency of 0.5 Hz does not have the same effect. Another study indicated that pain relief was more effective with rTMS at a frequency of 20 Hz compared to 1 Hz. The findings of a third study indicated that 10-Hz rTMS showed greater efficacy compared to 5-Hz rTMS, while 1-Hz rTMS did not produce significant effects. When assessing the pain-relieving effectiveness of rTMS in chronic pain, it is crucial to consider various factors that can influence the results, including the frequency, location, duration, and timing of the stimulation **(Lefaucheur et al. 2008).**

The study conducted by **Lefaucheur et al.** presented different results compared to the current research. They found that the pain-relieving benefits of applying rTMS to the primary motor cortex can last up to 6 months in people with chronic pain. However, their study focused on individuals with fibromyalgia, whereas our research investigated individuals with radicular pain. The researchers theorized that a decrease in pain severity was associated with a lasting enhancement in various clinical factors, such as fatigue and several aspects related to quality of life. They proposed that the pain-relieving advantages of M1 rTMS on individuals with fibromyalgia were connected to changes in intracortical modulation, which might play a role in the mechanisms responsible for its pain-relieving effects. ***(Mhalla et al. 2011).***

The researchers proposed that a decrease in pain severity could be associated with a lasting enhancement in various clinical aspects, including tiredness and several elements related to quality of life. They also suggested that the pain-relieving effects of M1 rTMS on individuals with fibromyalgia might be connected to changes in intracortical modulation, which could play a role in the mechanisms underlying its analgesic properties. The pattern of stimulation included 10 sets of 10-second durations, with a 30-second break between each set. This amounted to a total of 2000 pulses delivered within a session lasting 6-7 minutes. The group receiving real rTMS outperformed the sham group in terms of pain intensity ratings, experiencing an average reduction of 35-40% two weeks following the final session. However, the positive effects diminished after one month ***(Khedr et al., 2015).***

The findings of the present study confirm that the location of stimulation plays a crucial role. Specifically, stimulating the hand area of M1 proves to be more successful in alleviating upper limb pain compared to stimulating the foot area of M1, which has no significant effect on lower limb pain. Additionally, it is possible that any pain-

relieving effects observed may be attributed to the placebo effect, as suggested by previous studies focusing on short-term effects **(Hosomi et al.2020)**.

Limitations of this study were that the participants represented a selected group of patients with unilateral lumbar radiculopathy, and unilateral lumbar radiculopathy which represent a localized part of radiculopathy that couldn't be generalized to the cervical radiculopathy and other neuropathic pain. So farther studies with follow up are needed. Patients had to come to the hospital every other day which accounts for drop outs. Corona virus pandemics and curfews were also one of the reasons that caused the number of the dropped out patients.

Finally, according to the results of the current study, rTMS didn't show any significant effect on relieving pain due to lumber radiculopathy.

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