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A prospective study to evaluate the role of repetitive trans-cranial magnetic stimulation in treatment of chronic low back pain

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ABSTRACT

Introduction: Chronic Low Back Pain (CLBP) is a disabling musculoskeletal condition with a high prevalence in developing and developed countries. There are many treatment modalities but none of them provides a satisfactory and consistent cure. Recently focus has shifted to neuromodulation to cure chronic pains. The U.S. Food and Drug Administration (FDA) approved the use of Repetitive TMS (rTMS) in the management of Pain in 2013. Since then, centres across the world have been using Transcranial Magnetic Stimulation (TMS) as a noninvasive modality for the treatment of various pain conditions. rTMS is a variation of TMS where stimulation is provided in sessions to create long-term excitation in the brain cortex. Evidence on the effectiveness of rTMS for CLBP is scarce due to limited rigorous clinical trials. This study is the first of its kind undertaken in India to critically analyze the role of rTMS in the treatment of CLBP.

Materials & Methods: In this single institutional prospective, single-blind study, we enrolled 40 patients of CLBP sharing similar clinical profiles. They were divided into a test group and a sham group. In the test group patients were given rTMS in addition to conventional treatment while in the sham group, patients were taken through the procedure of rTMS without actually being administered it. A figure-of-eight-shaped coil was used focusing on the Left M1 area and Dorsolateral prefrontal cortex to administer the rTMS by a trained physician. Visual Analogue Scores (VAS) were noted before and after the procedure. Each patient was continuously monitored during the procedure for any side effects. Subsequently, they were interviewed and followed up for 6 months. At the end of 6 months, data was compiled and conclusions were drawn.

Result: In our study, we found that 90 per cent of patients in the test group reported a reduction in VAS score by 30 per cent reduction while the remaining had a 20 per cent reduction in pain scores. 90 per cent of subjects in the sham group reported a marginal improvement in VAS score which can be attributed to the placebo effect. Most patients in the test group reported an improvement in quality of life at the end of six months. None of the patients suffered any untoward side effects during or after the procedure.

Conclusion: Based on our study we conclude that rTMS is a safe procedure and it can be used as a modality in treating CLBP with satisfactory outcomes. Although the sample size was small, it is the first study of its kind undertaken in India to evaluate the role of rTMS-based neuromodulation in treating this chronic disabling condition. However, to be accepted as a standard of care for CLBP it will require further multi-institutional robust clinical trials with long-term follow-up.

Keywords
repetitive trans cranial magnetic stimulation (RTMS), chronic low back pain (CLBP), neuromodulation

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1. Introduction and Background

Low back pain (LBP) refers to pain, muscle tension, or stiffness that occurs below the costal margin and above the inferior gluteal fold, with or without sciatica (pain that spreads from the lower back down to the legs.[1] LBP persisting >3 months is termed as CLBP. Low back pain is one of the most common musculoskeletal diseases among people with chronic pain. Recent research reveals about 45–75% of patients report feeling pain 12 months after the onset of LBP.[2] Lifetime prevalence of low back pain (LBP) is over 70% in industrialized countries with a worldwide lifetime prevalence of 84%.[3] There are many modalities for treating LBP like muscles strengthening exercises, nerve root block and analgesics, despite established benefits of these methods many patient face refractory low back pain. With increasing CLBP prevalence the affected individuals are persistently visiting the health care facilities resulting in loss of working hour and cost to the state and severly diminishing individuals activities of daily living (ADL). Recently focus has shifted on use of Transcranial Magnetic Stimulation (TMS) as a noninvasive modality for treatment of CLBP. The exact mechanism of TMS has not been understood however, it is hypothesized that TMS effects neuromodulation of brain tissue through the production of the high or low-intensity magnetic field to modulate cortical excitability.[4] rTMS refers to applying recurring TMS pulses to a specific brain region(motor cortex). rTMS is a variation of TMS where stimulation is provided in sessions of same condition to create long-term excitation in the brain cortex. The electromagnetic induction generated by rTMS is painless and safely passes through the skin and skull. Then, it produces small electric currents in the region of the brain just under the coil.[5]

rTMS has been approved by the U.S Food and Drug Administration (FDA) for the treatment of major depressive disorder (MDD) by 2008, While approval for treating pain was granted in 2013. Of late, various neurostimulation methods, including rTMS, peripheral nerve stimulation, spinal cord stimulation, deep brain stimulation, and motor cortex stimulation, have been applied to chronic-pain treatments including patient of Chronic low Back ache (CLBP). However, evidence on the effectiveness of rTMS for CLBP is scarce due to limited rigorous clinical trials. The aim of this study is to critically analyze the role of rTMS in treatment of CLBP in Indian population.

2. Material & Methods

2.1 Study Protocol: A Prospective, single center study conducted at Department of Neurosurgery and Department of Psychiatry at Command Hospital SC, Pune from Jan 2023 to June 2023. Total 40 patients of chronic low back pain sharing similar clinical profile were included in this study, with 20 patients in Test group & 20 in Sham group. The Test group was subjected to High frequency rTMS of 15 to 20 Hz, for 20 minutes in each session (6 sessions given per patient within 6 weeks), Sham group underwent the placement of coils without actually giving rTMS.

2.1.1 Inclusion Criteria:

1. Participants aged above 18 years;
2. Willing to participate in the study
3. Having stable pharmacological or nonpharmacological treatments for pain.
4. Low backpain more than 3 months

2.1.2 Exclusion Criteria

1. Specific causes: Autoimmune disease, Inflammatory, infective, malignancy, trauma (e.g., spondylosis, spondyloarthropathy, or vertebral fracture);
2. Pregnancy or nursing female
3. Previous spinal surgery
4. Psychiatric Illness
5. Evidence of Prolapsed disc on MRI imaging
6. Contraindications to use rTMS (e.g., severe head trauma, intracranial hypertension, implanted ferromagnetic devices, history of epilepsy).

2.2 Methodology:

All patient underwent MRI LS Spine before being enrolled for rTMS to exclude inflammatory, infective cause of LBP and prolapsed disc. After obtaining informed written consent, a figure-of-eight-shaped coil was used focusing on Left M1 area and Dorsolateral Pre-Frontal Cortex(Fig-1 & Fig-2). Motor evoked potential was recorded by observing the twitching of right thumb visually, for each patient and frequency of pulse which generates twitching was recorded and frequency which is lesser than Motor Evoked potential for each session was applied. Frequency given to each patient ranges between 20

Hz for 20 mins (total 06 sessions, once per week). Vitals of each patient was monitored pre and post session. Each patient as given a visual analogue scale (VAS) at end of each session and at the end of six weeks. Score of each session was recorded at end of each session and at end of 06 weeks. All patients were followed up for 6 weeks post rTMS for any procedure complications.

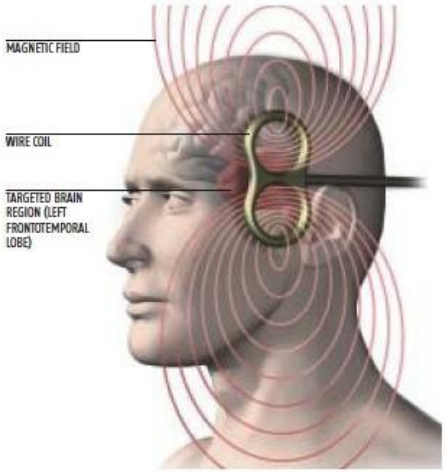

Figure 1. (left) / **Figure 2**. (right)

2.3 Ethical Clearence: (certificate enclosed) was taken by institutional ethical committee and all participants consent was obtained prior to study

Table 1. Pre and Post rTMS VAS

	Group							
	Test group			Sham group				
	Mean	Median	Std. Deviation	Mean	Median	Std. Deviation	p Value	Significance
Pre Procedure VAS	10.00	10.00	0.00	10.00	10.00	0.00	1.000	Not Significant
Post Procedure VAS	7.17	8.00	1.72	8.55	9.00	0.82	<0.001	Significant
Change in VAS	2.83	2.00	1.72	1.45	1.00	0.82	<0.001	Significant
% Change in VAS	28.26	20.00	17.23	14.50	10.00	8.20	<0.001	Significant

The pre procedure VAS was 10 in both the Test and Sham Group however the Post procedure VAS obtained after 04 sessions of rTMS statistically significant reduction in LBP with change in Mean VAS score of 28.26% in Test group compared to no change in Sham group (Table 1.).

Table 2. Change in VAS

		Group			
		Test group	Sham group	p Value	Significance
% Change in VAS	NO CHANGE	0(0)	02(10)	<0.001	Significant
	CHANGE <=30%	12(60%)	18(90)		
	CHANGE >30%	8(40%)	0(0)		
Total		20(100)	20(100)		

In our study we found that all patients in test group reported a reduction in VAS score in which 08 patients (40%) reported ≥30 percent reduction and 12 patients(60%) reported around 20% reduction in pain scores. However, 90 percent subjects in sham

group reported a marginal improvement in VAS score which can be attributed to placebo effect. Most patients in test group reported an improvement in quality of life (Table 2.)

Table 3. Post Procedure Complications

		Group		Total		
		Test group	Sham group		p Value	Significance
Complication	Headache	2(10)	1(5.2%)	3(8.1%)	0.577	Not Significant
	NONE	18(90)	19(94.8%)	37(91.9%)		
Total		20(100)	20(100)	40(100)		

Post procedure 02 patients (10%) in test and 01 Patient (5.2%) in Sham group reported with mild episodic headache which relieved with analgesics without requirement of further management (Table-3).

Table 4. Related studies on rTMS effect on CLBP

Author	Year	Subject	Sample Size	rTMS Protocol	Outcome
Ambriz et al [8]	2016	CLBP	n=82,rTMS-44,Sham-12, PT-26	10biphasic pulse/10sec at 20 Hz	Significant reduction in pain score
Lee et al [9]	2019	CLBP	n=21,rTMS-11, Sham-10	10 Mins, 10 Hz	Improvement in pain score in Test group
Olechowski et al [10]	2020	CLBP	n=20	20 mins, 10 hz	Long term improvement in Pian
Masoumbeigi et al [11]	2021	CLBP	n=09	40 Pulse, 28 sec rest period, 20 Hz	Reduction in VAS Score
Present Study	2023	CLBP	n=40, rTMS-20, Sham-20	1 session per week, 20 hz for 20 mins, Total 04 sessions	Statistically significant reduction in Post procedure VAS score

3. Statistical Analysis

The statistical software SPSS version 25 has been used for the analysis. Continuous variables are expressed as Mean, Median and Standard Deviation and compared across the groups using Mann-Whitney U test since the data does not follow normal distribution. Categorical variables are expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

4. Results

The demographic profile was comparable in both the groups with mean age is 39.26 and 39.05 in Test & Sham group respectively. In test group(n=20) 5 patients were female (21.74%) and 15 were male (78.26%) where as in Sham group(n=20) 7 Patients were female (26.67%) and 13 were male (73.33%).

5. Discussion

TMS is based on the Faraday law. As per recent understanding an electromagnetic coil sends a perpendicular magnetic field into the region of interest on the scalp. The mechanism of cortical stimulation for pain relief is believed to be due to the modification of neuronal excitability. rTMS is hypothesized to induce alterations in the activity of cortical and subcortical brain structures that are related to pain modulation and processing, including the orbitofrontal cortices, medial thalamus, anterior cingulate, and periaqueductal gray matter. Also, rTMS is hypothesized to reduce chronic pain by triggering descending inhibitory neural pathways which acts at dorsal-horn level. Other proposed mechanism of action include increase in cerebral blood flow to the affected areas as it is hypothesized

that patients with chronic pain have a decreased blood flow(12).. Broadly, rTMS has been classified, High frequency (>1 Hz) and Low frequency (<5Hz).[6] Stimulation frequency is associated with synaptic changes; higher frequencies (> 5 Hz) are excitatory, and lower frequencies (< 1 Hz) are inhibitory.[7] Numerous studies have established that active high-frequency rTMS (HF-rTMS) ranging between 5 Hz to 20 Hz has analgesic effects in management of chronic pain.[12,13] Findings of this study is consistent with results of previous studies which showed a significant reduction in pain score in patients undergoing rTMS Repetitive transcranial magnetic stimulation can be performed as an outpatient procedure for chronic low back pain. At present there are few studies which have evaluated efficacy of rTMS in patients with CLBP.

6. Conclusions

Based on our study we conclude that rTMS is a safe procedure and it can be used as a modality in treating CLBP with satisfactory outcomes. Although the sample size was small, it is the first study of its kind undertaken in India to evaluate the role of rTMS based neuromodulation in treating this chronic disabling condition. How ever to be accepted as a standard of care for CLBP it will require multi-institutional robust clinical trials with long term follow up.

Limitations: Single centre and single blinded study with small sample size.The reproducibility of results post rTMS can be further studied with multicenter study on larger population and long term follow up is required to observe for late onset complication if any.

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