Cover page study protocol

Study Title: Application of transcranial magnetic stimulation treatment in patients with oncological neuropathic pain to evaluate effectiveness on pain and quality of life

NCT number: 05480410

Date of the document: 1/02/2022

Study protocol

The protocol will be structured according to the national institute of health, the statements described by the clinical trial database and the SPIRIT declaration, which include detailed study description and design, intervention, outcome measures and individual participant data and results sharing statement.

10 patients will receive 20 sessions of transcranial magnetic stimulation using the MagVenture Mag Pro R20 device. These sessions will be conducted daily from Monday to Friday, lasting 20 minutes each, at an intensity of 81% with a motor threshold of 90 A/ns.

A pre-post design without a control group will be used to evaluate 2 elements: pain and quality of life.

The evaluation moments will be as follows:

- Pretest: Quality of life and pain will be assessed using the Visual Analog Scale (VAS) and the Brief Pain Inventory (BPI).
- Each session: Pain will be assessed using the VAS.
- Each week: Pain will be assessed using the BPI.
- Immediate Posttest: Quality of life and pain will be assessed using both scales.
- Posttest at 1 month and 3 months: Quality of life and pain will be assessed using both scales.

The patients will meet the following inclusion criteria: female or males aged over 18 and under 75 years, any stage of cancer, chemotherapeutic treatment consisting of taxanos or oxaliplatin, neuropathic pain with a minimum grade 2 severity based on the National Cancer Institute Common Terminology Criteria for Adverse Events scale (NCI-CTCAE, version 5.0), and a mean 2 score or above in a visual analogue scale (VAS) of pain. We will exclude patients with any psychiatric disorder including major depression; history of seizure, epilepsy, stroke and intracranial metallic devices. Patients should agree to avoid any extra use of medication or to make any changes to their pharmacological plan during the trial.

The aim of collecting these variables is to gather data and conduct statistical analysis to evaluate the effectiveness of transcranial magnetic stimulation on pain and quality of life in patients with neuropathic pain secondary to oncological treatment.

TEST 1: Pain

This symptom will be evaluated using the Visual Analog Scale for pain and the Brief Pain Inventory (BPI), questionnaires that have been previously used in oncology populations (Goto et al., 2020; Khedr et al., 2015).

The Visual Analog Scale is rated from 0 to 10, where 0 indicates no pain and 10 represents the maximum pain.

The Brief Pain Inventory allows patients to rate the severity of their pain and the extent to which their pain interferes with their functionality.

An average is calculated for the elements that compose the pain severity category (worst pain, least pain, average pain, and current pain) and the elements that compose the pain interference category in functionality (interference in mood, walking, working, social interactions, sleeping, and enjoyment of life). Higher averages indicate worse patient condition.

Test 2: Quality of Life

Quality of life will be assessed using the Functional Assessment of Cancer Therapy FACT-GOG-NTX 13 scale, which has been psychometrically analyzed and validated in oncology populations (Cheng et al., 2020).

This scale includes 5 categories:
- Physical Well-being
- Social Well-being
- Emotional Well-being
- Functional Well-being
- Neurotoxicity

For scoring the scale, the ratings of these categories are summed, a higher total score means a better quality of life.

Determination of resting motor threshold

The target stimulation will be the primary motor cortex in its subdivision representing the hand; for this process, a basic trained operator identify the 'omega-shape' sulcus defining the Rolandic sulcus. Other authors have reported this specific hot spot target including the expert consensus established by a group of European experts, they described a Level A recommendation for the use of M1 as stimulation site for analgesic effect. Then the accurate position of the target will be adjusted according to the amplitude of the motor response on the contralateral hand, which a basic rTMS-trained physiotherapist will confirmed. This target has been shown in different investigations, to have greater specificity and effectiveness in the treatment of neuropathic pain. Once the target will be identified, it should be marked on a cap for the following sessions. A physiotherapist will be present weekly for assessment and to supervise patients' responses to treatment.

The occurrence of adverse events will be noted throughout the study period.

Cover page Informed consent

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INFORMED CONSENT

Study Title: Application of transcranial magnetic stimulation treatment in patients with oncological neuropathic pain to evaluate effectiveness on pain and quality of life

Project Code SIGP: 013008028-2021-311

DATE: _____

SUBJECT DETAILS	
Subject No.	
First Name	
Last Name	
Full name	
Identification document	

INFORMED CONSENT

This document authorizes the application of transcranial magnetic therapy as a treatment for pain management in oncological patients, provided through a collaboration between Neuro Clínica CORTEX SAS and Fundación Universitaria María Cano. The purpose is to evaluate the effectiveness of transcranial magnetic stimulation intervention on pain and quality of life.

A total of 20 sessions of Transcranial Magnetic Stimulation will be conducted using the MagVenture Mag Pro R20 equipment. The interventions will be supervised and evaluated through questions related to pain classification, description, functionality, ability to perform daily activities, and quality of life. These assessments will include pre-tests, after each session, immediate post-tests, and follow-ups at one month and three months post-intervention. Demographic and personal information will also be collected. Each session will last 20 minutes and will be conducted within a tolerance level of 81% with a motor threshold of 90 A/ns.

Information provided by the patients will be stored electronically and physically. The volunteer may authorize or refuse participation in this intervention after understanding the benefits and risks explained below.

GENERAL INFORMATION

You have been invited to participate in a research study on the effectiveness of transcranial magnetic stimulation on pain and quality of life.

Procedure

In the first part of the study, you will be asked a series of questions about your daily activities, how you perform them, the duration of your pain experience, and how you describe and classify it. The interview and intervention will focus on pain management and its impact on your quality of life. Each session will last 20 minutes.

Application of physiotherapy treatment protocol

The focus will be on evaluating the effectiveness of transcranial magnetic therapy on neuropathic pain.

Your decision to participate in this study is completely voluntary, and you may choose to continue or withdraw from the intervention or abstain from answering questions you do not wish to answer without penalty. If you choose not to complete the intervention, you may inform the researcher at any time.

Confidentiality

Your participation in this study is completely confidential, and the information provided will be analyzed under a unique identification number along with evaluations and interventions conducted on other patients, reported in aggregate form without mentioning personal or identifying information. Information collected in this study will be used for teaching, research, publications, or presentations at scientific events.

Benefits

While the research may not directly benefit you personally, nor provide any economic benefit for participating, the research findings may contribute to the development of alternatives in the treatment of oncological patients with neuropathic pain. The assessments and subsequent analysis will help address certain aspects impacting pain management and thus the quality of life of users.

Risks associated with the Intervention

As this is a quantitative study with a quasi-experimental, descriptive correlational design, pre-post without a control group, a standardized therapeutic protocol will be implemented to evaluate the effectiveness of transcranial magnetic therapy in reducing pain. According to Resolution No. 8430 of 1993, the risk classification is minimal, given that the procedure is under evaluation and application of a treatment protocol. However, there may be mild headaches, dizziness, and/or drowsiness, which are manageable and only probable.

Investigators

At least one of the following investigators will be present during the intervention:

Name	Role	Institution
Catalina Lopera Muñetón	Main investigator	FUMC
Isabel Cristina Ángel Bustos	Coinvestigador	FUMC
Dionis Vallejo Mesa	Investigador Externo	Rosario clinic

Contacts

If you have any doubts, complaints, or suggestions about the project, you can contact the investigators at their respective emails:

Investigator	Phone	Email
Catalina Lopera Muñetón	3206728934	catalinaloperamuneton@fumc.edu.co
Isabel Cristina Ángel Bustos	3146185960	Isabelcristinaangelbustos@fumc.edu.co

VOLUNTARY CONSENT

I, _____

Identified with citizenship ID No. _____

declare that I attend this session/intervention as an autonomous user, freely and voluntarily, exercising my faculties. Likewise, having been informed about the purposes, objectives, and procedures to be carried out during the project "Application of transcranial magnetic stimulation treatment in patients with oncological neuropathic pain to evaluate effectiveness on pain and quality of life," I authorize my participation in it and the use of the data obtained for academic and research purposes.

Additionally, I am informed that:

1. My participation in this research is completely voluntary, and I may withdraw at any time.

2. I will not receive any financial benefit of any kind for participating in this project. The research results obtained may contribute to the development of alternatives for pain management and thus the quality of life of users. The assessments and subsequent analysis will help address certain aspects impacting the quality of life of users.

3. All information obtained and research results will be treated confidentially. This information will be archived in paper and electronic format. Study files will be kept under the custody of the FISIOTER group of Fundación Universitaria María Cano, Neuro Clínica CORTEX, and the responsibility of its researchers.

4. Since all information in this research project is anonymized, personal results cannot be made available to third parties such as family members, employers, governmental organizations, insurance companies, or other educational institutions.

5. In case my personal data, photographs, and videos are required for events such as seminars, congresses, clinical case reviews, and publications, I authorize their use through the signing of this document. It is clarified that no individual identification data of participants will be presented.

I certify that I have read and understood this entire document. Therefore, I confirm that I have been satisfactorily informed about the processes to be carried out by the professionals, and I give my consent.

"I declare that I have not received verbal, written, and/or gestural pressures to participate in the study; that this decision was made in full use of my mental faculties, without being under the influence of medications, drugs, or alcohol, consciously, autonomously, and freely."

[Signature] _____

[Date] _____