DOI: 10.7860/JCDR/2024/67219.19270

Research Protocol

Dentistry Section

Effectiveness of Photobiomodulation Alone and 0.5% Nanocurcumin Gel with Photobiomodulation in Treating Myogenous Temporomandibular Disorders: Protocol for a Randomised Clinical Trial

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ABSTRACT

Introduction: Temporomandibular Disorders (TMD) encompass a variety of clinical dysfunctions affecting the Temporomandibular Joint (TMJ), masticatory muscles, and nearby tissues. Pain typically originates from the muscles associated with the functional movements of these structures. Low-level Laser Therapy (LLLT) has been used in TMD patients to control inflammation and disrupt the stress-pain-stress cycle. Curcuma longa is a significant plant in Asia used for medicinal purposes. Curcumin (diferuloylmethane) is a hydrophobic bioactive compound commonly found in the rhizome of C. longa. Considerable attention has been given in recent years to its various pharmacological actions. The available research has shown significant potential in inflammation control, with nano-range preparations of curcumin (Nanocurcumin) enhancing the pharmacological actions and benefits of curcumin, which were not markedly achievable before.

Need for the study: The TMDs are among the most common types of disorders associated with orofacial pain. Conditions originating from stress related to the joint often impact the associated muscles, initiating the stress-pain-stress cycle. As TMDs do not have a definitive treatment plan, further research is needed regarding the treatment associated with TMDs.

Aim: To assess the effectiveness of photobiomodulation alone and 0.5% nanocurcumin gel with photobiomodulation in treating myogenous TMDs.

Methodology: In the present randomised clinical trial, 44 patients with myogenous TMDs will be included. The patients will be divided into two groups: Group A will receive laser applications at the trigger zones, and Group B will receive the application of 0.5% nanocurcumin gel along with laser at the trigger zones. Patients will be assessed for jaw opening, Beck's Anxiety Inventory, and Visual Analogue Score after four weeks.

Keywords: Diferuloylmethane, Inflammations, Photobiomodulation therapy

INTRODUCTION

Considered the foremost reason for non dental facial pain, TMDs involve a large variety of mastication muscles and TMJ symptoms with a prevalence of 20-25% among adolescents [1]. Multifactorial aetiology, lack of diagnostic parameters, and the inability of patients to locate the pain in the TM Joint regions are the primary causes of delay in diagnosis. The Visual Analogue Scale (VAS) score and mouth-opening analysis are the most used tools for analysis. However, aspects like chronic pain, depression, and anxiety are neglected. Therefore, the Research Diagnosis Criteria for TMD (RDC/TMD) has been developed and used worldwide as the gold standard [1]. Myogenous TMDs are the type of TMDs associated with the joint's muscular component. The muscles attached to the TMJ aid in the opening and closing of the joint. Often, after a stressful event on the muscles, they initiate the stress-pain-stress cycle, leading to pain in the muscular component of the joint [1].

Therapies like Photobiomodulation Medical care (PBM) aim to alleviate TMD symptoms. Treatment of photobiomodulation involves using an optical laser to reduce inflammation, pain, oedema, and regeneration of broken tissues like bones [1,2]. It includes the photo absorption by the natural group cytochrome enzyme catalysing the metabolic oxidation-reduction reaction, increasing metabolism, which ends in the proliferation of cells, inhibitor and redox-regulation, hindrance of necrobiosis, restoration of metabolism of cells, and reducing pain and inflammation [1,2]. Photobiomodulation has been previously used in many studies [1-4] associated with TMDs and myofascial pain dysfunction syndrome and has shown promising results while using photobiomodulation alone and in combination with diclofenac gel. Thus, photobiomodulation was considered as the treatment modality.

Curcumin (diferuloylmethane) is a hydrophobic bioactive element that is commonly found in the rhizome of C. longa [5,6]. Upon searching various databases, the study material available on using nanocurcumin in treating myogenous TMD was minimal, as only a few studies were performed with the following material (nanocurcumin) in treating osteoarthritis and orofacial pain [7-10]. Most treatments associated with nanocurcumin were performed for pain and inflammation associated with knee joints. Thus, nanocurcumin was considered the material of choice for the present study.

Literature is sparse on the use of combination therapy of photobiomodulation with curcumin in TMDs. Thus, the present study aimed to compare the effectiveness of photobiomodulation and nanocurcumin, alone or combined (0.5%), in treating TMD pain.

Objectives

Assessing the effectiveness of photobiomodulation alone in treating myogenous TMDs. To assess the effectiveness of 0.5% nanocurcumin gel with photobiomodulation in treating myogenous TMDs. To compare the effectiveness of photobiomodulation alone and 0.5% nanocurcumin gel with photobiomodulation in treating myogenous TMDs.

REVIEW OF LITERATURE

Brochado FT et al., conducted a study on the effectiveness of photobiomodulation in the treatment of TMDs [1]. The study evaluated parameters involving the intensity of pain, movements of the mandible, aspects of social and psychological factors, and symptoms related to anxiety in TMDs. A total of 51 patients were randomly assigned to three groups: Group 1, with 18 patients receiving laser; Group 2, with 16 patients receiving physiotherapy for 20 minutes for mastication and joint muscles; and Group 3, with 17 patients receiving combination therapy. All groups showed reductions in pain, and jaw movements improved during treatment and at follow-up.

A study evaluating the effects of photobiomodulation on the transdermal absorption of diclofenac in healthy volunteers was conducted by Leonardo PS et al., [2]. After assessing their health status, volunteers were selected based on the criteria of 12 with black skin and 12 with white skin, and the study was initiated for the determination of pharmacokinetic parameters. During hospitalisation, the volunteers were given 5 grams of diclofenac in gel form with or without photobiomodulation following randomisation. A fourteen-laser diode cluster delivered energy to each diode. Haematological samples were obtained to determine the plasmatic diclofenac concentration using tandem mass spectrometry at various time points. The effective wavelength of 650 nm enhanced the absorption of diclofenac gel, favouring white-skinned individuals but not those with black skin. The white-skinned volunteers who received low-level lasers before the drug application showed significant improvements compared to those who received a placebo.

A study investigating the penetration and the effects against neoplastic activities of curcumin using liposomes for transdermal delivery was conducted by Chen Y et al., [5]. Phospholipids (soybean, egg yolk, and hydrogenated) were used to prepare the liposomes, which were loaded with curcumin. Soybeans promoted drug permeation and deposition most significantly, followed by egg yolk, hydrogenated, and curcumin solution.

Malekzadeh M et al., conducted a study on the effects of nano-curcumin on the gingiva in patients with gingival and periodontal involvement [6]. A total of 48 patients were selected. One group received curcumin, and a placebo was given to the other. The assessment was done on the gingiva, papilla, and plaque indices. Both groups showed promising improvements, which were even better in the curcumin group, with no side-effects.

The study conducted by Zhang Z et al., evaluated the use of curcumin in treating osteoarthritic progression and associated pain [7]. The evaluation of cartilage degradative-associated genes was performed using real-time Polymerase Chain Reaction (PCR) assessment of curcumin and curcumin nanoparticles in human primary chondrocytes. Mice subjected to Destabilisation of the Medial Meniscus (DMM) surgery were orally and topically administered nanoparticles for eight weeks. Both forms of curcumin suppressed the messenger Ribonucleic Acid (mRNA) expression of proinflammatory mediators Interleukin-1β (IL-1β) and Tumour Necrosis Factor-α (TNF-α), as well as MMPs 1, 3, and 13. Significant improvement was observed in both oral and topical administration, with topical oral administration showing better results than oral.

MATERIALS AND METHODS

The randomised controlled clinical trial will be conducted at the Department of Oral Medicine and Radiology and the Department of Periodontics at Sharad Pawar Dental College, DMIHER, Sawangi, (M) Wardha, Maharashtra, India. The study protocol has been approved by the Institutional Ethics Committee and registered with CTRI NO: REF/2022/06/055852. The study protocol will be explained to the participating patients, and written informed consent will be obtained from them (https://ctri.nic.in/Clinicaltrials/main1.php?EncHid=39494.39456).

Inclusion criteria: Patients with myogenous TMDs will be included. Patients will undergo examination for TMDs based on clinical inspection and palpation of the joint and muscles of mastication. A study orthopantomogram will be taken to exclude patients with bony aetiologies. Once myogenous aetiologies are confirmed, patients will be considered for the study.

Exclusion criteria: Patients with bony pathologies of the TMJ, a history of facial trauma, congenital developmental anomalies, and malignancies will be excluded from this study.

Sample size calculation: The sample size was calculated using the following formula:

$$n=\frac{x^2,N.P(1-P)}{c^2\,(N-1)+22.P.\,(1-P)}$$

Where:

X=Chisanare tabulated value for one degree of freedom at a 95% confidence interval=3.84

P=Proportion of 50%=0.50

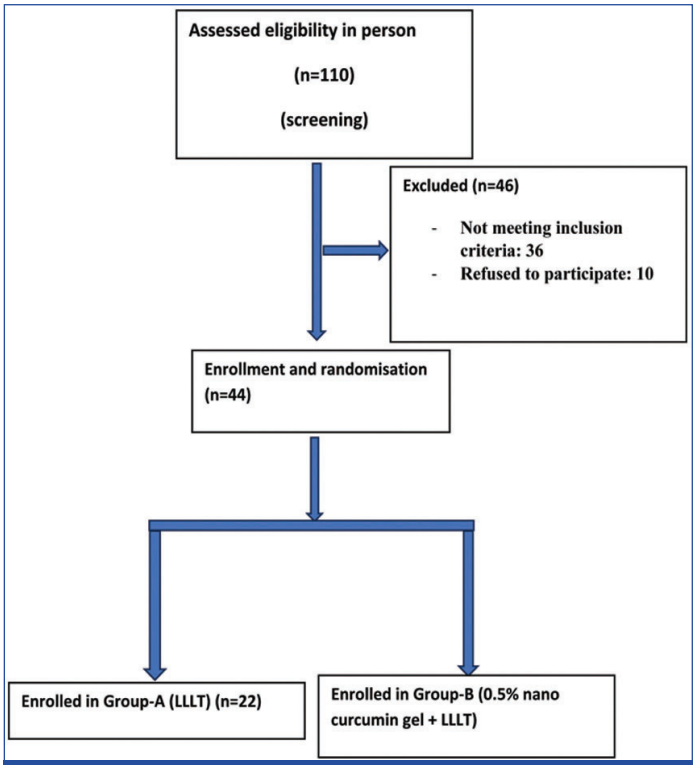
N=Total number of patients, i.e., 50

C=Desired margin of error=5%=0.05

n=44.34

n=44

The flow diagram depicting the distribution of study participants has been presented in [Table/Fig-1].



[Table/Fig-1]: Disribution of study participants.

Study Procedure

After informing the patient about the study, consent will be obtained. Following the detailed case history as per the prescribed proforma, all necessary findings such as pain-free jaw opening, Visual Analogue Score (VAS) and Beck's Anxiety Inventory (BAI) index [1] will be noted. The zones with the maximum discomfort from which the pain originates will be analysed based on the patient's history and manual palpatory examination (Trigger Zones).

To avoid selection bias, a chit system will be used to select the patient. The chits will be drawn by someone other than the patient or clinician. The clinician will be informed about the group allocation, and the patient will be blinded.

According to the allotted chit, the patient will be assigned to one of the following groups:

1) Group A-LLLT only (GaAlAs diode laser, 800-900 nm. Biolase, Foothill Ranch, CA, USA.)
2) Group B-0.5% nanocurcumin gel (Sigma-Aldrich, St. Louis, Missouri, USA) + LLLT (GaAlAs diode laser, 800-900 nm. Biolase, Foothill Ranch, CA, USA.)

Group A will receive laser application at the trigger zones thrice per week for four weeks, following the specified schedule (GaAlAs diode laser of wavelength 880 nm and 0.8 W power, Time: 4 minutes. Biolase, Foothill Ranch, CA, USA.)

Group B will receive applications of 0.5% nanocurcumin gel (Sigma-Aldrich, St. Louis, Missouri, USA) at the trigger zones thrice per week for four weeks. The application of low-level laser will follow the schedule as specified (GaAlAs diode laser of wavelength 880 nm and 0.8 W power, Time: four minutes. Biolase, Foothill Ranch, CA, USA.)

After four weeks, the patients will be evaluated for pain-free jaw opening, VAS, and BAI. All groups will be examined, and data will be collected for comparison at the end of the study.

Primary outcome: According to the reviewed observations from various studies, the combination therapy will be more effective than the photobiomodulation therapy alone. The expected dose of laser will be reduced significantly and the drug penetration will be improved after encountering laser. It will be more effective in reduction of pain, as well as improving the pain free mouth opening.

Secondary outcome: The number of visits that are required in combination therapy will be lesser as compared with photobiomodiulation therapy alone.

STATISTICAL ANALYSIS

The gathered data will be analysed using Statistical Package for Social Sciences (SPSS) 27.0 Version software. Descriptive and analytical statistical methods will be employed for data analysis. The statistical significance of the mean differences between the pain levels on the VAS, pain-free jaw opening, and BAI will be examined on the same day, the 15th day, and one month later, and will be compared between both groups (i.e., Group A and Group B).

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Aug 26, 2023
- Manual Googling: Oct 21, 2023
- iThenticate Software: Feb 24, 2024 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 8

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 25, 2023**
Date of Peer Review: **Oct 19, 2023**
Date of Acceptance: **Dec 30, 2023**
Date of Publishing: **Apr 01, 2024**