

BMJ Open Photomodulation in the treatment of chronic pain in patients with temporomandibular disorder: protocol for cost-effectiveness analysis

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ABSTRACT

Introduction Epidemiological data show that the signs and symptoms of temporomandibular disorder (TMD) start becoming apparent from 6 years of age, and during adolescence these signs and symptoms are similar to those of adults. The present study aims to estimate the direct costs for treatment of chronic muscle pain with photobiomodulation therapy, occlusal splint and placebo in patients with TMD; to evaluate the effectiveness of photobiomodulation therapy and occlusal splint for treatment of muscle pain in patients with TMD; to analyse the cost-effectiveness of the two proposed treatments for pain; and to describe and compare the results of the analyses of these treatments.

Methods and analysis This is a prospective trial of clinical and economic analyses that will include 135 patients with TMD aged between 15 years and 25 years, randomly assigned to a treatment group: G1 (photobiomodulation), G2 (occlusal splint) and G3 (placebo). The analyses will be based on the cost of each treatment during the 12-month period. The outcome of the analysis of effectiveness will be pain, measured periodically by means of clinical examination of Research Diagnostic Criteria for Temporomandibular Disorders. The cost-effectiveness ratio will be calculated using, as end points, pain and the ratio of the differences in costs between the groups studied. The evaluation of the impact of the treatment on quality of life will be determined by applying the adapted EuroQol-5D.

Ethics and dissemination This protocol has been ethically approved by the local medical ethical committee, protocol number 2.014.339. Results will be submitted to international peer-reviewed journals and presented at international conferences.

Trial registration number NCT03096301.

INTRODUCTION

Temporomandibular disorder (TMD) is a term used to define a number of clinical signs and symptoms that affect the masticatory muscles, the temporomandibular joint (TMJ) and associated structures.^{1–6} The most

common signs and symptoms are sensitivity of the masticatory muscles, pain in one or both TMJs, limited mandibular movement, articular noises,^{6–8} headache,^{6,9,10} associated dizziness, hearing loss and sometimes tinnitus.^{1,11} Signs and symptoms of TMD are seen at all ages, however, the prevalence of this disorder, considered low in children, increases with age in adolescents and young adults.^{12,13} The changes caused by TMD, especially pain, can interfere with the quality of life of these patients.¹⁴

Various treatment options have been proposed, mainly for pain control, such as occlusal splints, acupuncture, kinesiotherapy, massage therapy, postural training, psychotherapy, joint mobilisations, drug therapy and laser therapy.^{15,16} Photobiomodulation therapy is a non-invasive, non-pharmacological treatment that, according to various studies, has shown beneficial results in the treatment of pain associated with TMD.^{4–7,16–24} Photobiomodulation is a radiation located between the visible and infrared portions of the spectrum of electromagnetic waves, with characteristics of monochromaticity, coherence, one-directionality and variable wavelength.⁶ Inflammation modulation and analgesic effects are cited among the therapeutic results of photobiomodulation treatment on TMD.^{5,6,22,25,26}

Laser therapy has demonstrated the capacity to assist in symptomatic treatment of pain, promoting a considerable degree of comfort for the patient immediately after its application. The main advantage of laser applications in the treatment of TMD is that this type of therapy is non-invasive and low-cost, and is currently widely used in dental clinics, reducing the demand for surgery or drugs

for the treatment of pain relief and tissue regeneration. The application of laser therapy in patients with TMD has demonstrated the ability to relieve pain within minutes of its application, promoting significant well-being. Moreover, it is an adjuvant pain-relief treatment in which the analgesic action of the laser enables the patient to return to their duties, providing more comfort and a better quality of life.^{5 6 22 25}

Occlusal splint is a device that is widely used in the treatment of TMD and pain control. The use of an occlusal splint can lead to improvement after 1 month and even decreased pain symptoms after 1 week of use.²⁷ Therapy with occlusal splints is the most widely used technique in dentistry for the treatment and control of pain in TMDs because it is considered to be a conservative and non-invasive treatment option.

Although clinical studies, demonstrating the benefits of both photobiomodulation treatment and occlusal splints for pain control, have been published, the cost of TMD in young patients or the cost utility of these two treatments has not been established. Cost-utility analysis is a method of comparing the benefits and costs of technology used in healthcare; the benefits are measured in terms of life utility.²⁸

METHODS

Overview

This study aims to evaluate the cost-effectiveness of photobiomodulation therapy and occlusal splint for the treatment of pain in patients with TMD aged 15–25 years. This is a controlled clinical study for greater transparency and quality of this research, and [table 1](#) provides the enrolment, intervention and assessment schedule following the

Standard Protocol Items: Recommendations for Interventional Trials.

The study activities will be conducted at the Clinic of the School of Dentistry of Universidade Nove de Julho (UNINOVE). The project will follow the regulatory standards for ethics research with humans and will be submitted to the institutional review board of the university. Data collection will begin on receipt of a favourable opinion and after signed informed consent by the participants and/or their guardians.

Participants

Patients between 15 years and 25 years of age selected at the Clinic of the School of Dentistry of UNINOVE will participate in the study. One hundred and thirty-five patients will be selected, following the sample calculation based on studies with photobiomodulation treatment and occlusal splints, using the DINAM V.1.0 program.

The sample size calculation was based on literature²⁹ and considering an average of the Visual Analogue Scale (VAS) in improving pain, pretreatment and post-treatment. The level of significance (α) being 5% with 80% power of the test, 42 patients were calculated per group. The sample size for this study is 135 patients (45 per group). Only those patients in the sample with a diagnosis of TMD will be included in groups Ia and Ib.

Patient and public involvement statement

The patients in the three groups will receive standard information about the steps of research but they will not be involved in the recruitment and conduct of the study. Data collection will begin on receipt of a favourable opinion and after signing of the informed consent form by the participants and/or their guardians.

Table 1 Schedule of enrolment, interventions and assessments of temporomandibular disorder (TMD) treatment

	Study period						Closeout 12 months
	Enrolment	Allocation	0 Baseline	01 month	03 months	06 months	
Enrolment:							
Eligibility screen	X						
Informed consent	X						
Allocation		X					
Interventions:							
Photobiomodulation therapy		X	X	X	X	X	X
Occlusal splint		X	X	X	X	X	X
Placebo		X	X	X	X	X	X
Assessments:							
Pain		X	X	X	X	X	X
Quality of life		X	X	X	X	X	X
Cost							X

0=baseline, t_1 =01 month after the treatment, t_2 =03 months after the treatment, t_3 =06 months after the treatment, t_4 =12 months after the treatment.

Screening procedures

For a diagnosis of TMD (temporomandibular disorders), the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) Questionnaire³⁰ will be applied before any intervention. In addition to the questionnaire, a specific clinical examination will be conducted, always by the same previously trained evaluator, in which the patient will be positioned sitting in a chair, with their feet flat on the floor and the Camper plane parallel to the ground. The exam will consist of palpation of the temporalis, masseter, digastric and medial pterygoid muscles, palpation of the TMJs, and analysis of mandibular movement, using a digital pachymeter (Digimess) to measure the vertical and horizontal movements and a stethoscope to check for noises, as well as an investigation of frequent headaches, facial pain, tiredness and difficulty while chewing, bruxism, psychological aspects of adolescence and parafunctional habits. The RDC/TMD Questionnaire will indicate the diagnosis of myofascial TMD and the clinical examination form will analyse the mandibular movements. The diagnosis of pain will be evaluated by VAS and quality of life will be determined by applying the adapted EuroQol-5D (an instrument for measuring quality of life).

Preclinical trial

Inclusion criteria

Young people between 15 years and 25 years of age with a diagnosis of TMD in groups Ia and Ib (chronic myofascial pain in accordance with RDC/TMD) will be included in the study.

Exclusion criteria

Group II (disk displacement of TMJ) and group III (arthralgia, arthritis, arthrosis) individuals with dental-facial anomalies who have undergone orthodontic or orthopaedic treatment of the jaws or psychological or physical therapy will be excluded. Individuals who were taking muscle relaxants or anti-inflammatory medications will also be excluded. These patients will be advised and referred for treatment, but will not participate in this study.

Randomisation

Participants will be divided into three groups, as shown in table 2.

For random distribution of volunteers with TMD, will be use the randomised computer-generated list. Before the first evaluation, each patient will receive one number to determine the group to which they are allocated.

Table 2 Distribution of participants into research groups		
Control	Participants	Therapeutic intervention
1	45	Photobiomodulation
2	45	Occlusal splint
3	45	Placebo

Procedures

The treatment protocols of photobiomodulation and occlusal splint presented in this study are based on clinical trials.^{8 16 29 31}

The participants in the three groups will receive standard information about TDM, the complex cause of the pain and the possible contributing factors. The patients will be counselled to avoid the possibly stress-induced habits such as grinding, clenching, nail-biting or biting on objects like pencils, excessive gum chewing, biting and/or sucking on the lip or cheek, and pressing and/or sucking on the tongue.³²

The baseline of this study will be 2 weeks after the patients have received standard information. Each treatment (G1, G2, G3) will start after 2 weeks; a patient not responding to the treatment (non-responder) will be excluded from the research sample, and offered alternative integral treatment suitable to their needs (involving psychologists, physiotherapists and so on). As these data are very important, the number of patients withdrawn from the study will be computed and included in the intention-to-treat (ITT) analysis. At the end of the research, all patients will be treated integrally to determine the major cause of this disorder.

Treatment with photobiomodulation

A gallium-aluminium-arsenide laser (Twinflex Evolution model, MM Optics) will be used for the photobiomodulation therapy. The laser therapy sessions will be performed in a reserved room next to the dental clinic offices, free from sound interference. At the time of the application, only the volunteer to be treated and the professional responsible for the treatment will be present, both wearing special glasses for eye protection. The tip of the laser will be coated with disposable transparent plastic (polyvinyl chloride (PVC)) (to avoid cross-contamination and for reasons of hygiene) and the facial site to be irradiated will be cleansed with 70% alcohol. During the applications the patient will remain seated, with the Frankfurt plane parallel to the ground.

Twelve laser applications will be applied, with two sessions per week. A wavelength of 780 nm, with an energy density of 25J/cm², a power of 50 mW and power density of 1.25W/cm², will be used for a duration of 20s per point, resulting in a total energy of 1J per point, using a conventional tip in contact with the skin, thus considering an area of 0.04cm², in accordance with the protocol.^{8 16 31}

The laser will be applied to three points of the masseter muscle (upper, middle and lower bundles) and one point in the anterior temporalis on each side of the face.^{16 31}

The patients will be called for follow-up visits at 1 month, 3 months, 6 months and 12 months after the last day of photobiomodulation therapy.

Placebo group

For the placebo group, all the measures described for group 1 (photobiomodulation) will be adopted, however the laser equipment will remain switched off, and a sound

same as that of the equipment will be simulated with a guide light on. The placebo group will also have the same follow-up visits as that of group 1.

Treatment with occlusal splints

Stabilisation splint made with hard acrylic fabricated for the maxillary arch is the type of occlusal splint used in this study. The splints will be made following the principles established by literature.¹ Alginate will be used to obtain the moulds of the participants' models. A 2mm acetate splint will be made, to be later replaced with acrylic resin,³³ and these splints will be adjusted in centric relation, to promote occlusal stability and disocclusion guide.³⁴ The group undergoing treatment with occlusal splints will be instructed to use the device during sleep, 8 hours every night. The splints will be checked after 2 weeks of use and adjusted, if needed. The patients will be asked to use the occlusal splints according to the instructions given to them and to return 3 months after the treatment. If by this visit the patient has not responded to treatment (non-responder), the researchers will offer an alternate treatment method, but these patients will be excluded from the research sample. The patients that have responded to the treatment will continue to use the occlusal splint and return for the 6-month follow-up visit.²⁹

Evaluation of pain

Muscle pain will be analysed by clinical criteria of the RDC/TMD Questionnaire. Clinical examination will be conducted periodically, and the parameters for analysis will be at intervals of 1 month, 3 months, 6 months and 12 months. We will use VAS to assess pain level.

Evaluation of the impact of treatment on quality of life

EQ-5D will be used to assess the impact of treatment on the quality of life of the participants. EQ-5D is a generic instrument for assessing the quality of life related to health. It has been developed in Europe, and translated and validated for several languages, including Portuguese.³⁵ Because it was developed for the purpose of determining a single cardinal indicator of the state of health, it can be used for both clinical evaluation and economic evaluation.

For this type of study, it is important that the instrument is short and simple, and represents dimensions relating to quality of life and health status.³⁶ Currently, the original version is called EQ-5D-3L, and another version, EQ-5D-5L, has been launched. EQ-5D-3L is composed of two stages, a questionnaire and a VAS. The questionnaire contains five questions that evaluate mobility, personal care, usual activities, pain or discomfort, and anxiety/depression. For each question, patients are asked to select the option that best reflects their conditions, selecting from three alternatives. The first alternative indicates the absence of problems, the second indicates some problems, and the third, severe problems. The instrument will be applied at intervals of 1 month, 3 months, 6

months and 12 months, when each group is called back for follow-up visits. The responses will be compared intra-group (same subject at the different follow-up intervals) and between groups.

Cost analysis

This phase of the study will consist of the quantification of resources, that is, determining the frequency of use of resources and materials during the treatment. It is a preliminary cost-effectiveness study, so we opted to analyse only direct costs. The units used to quantify the direct costs consumed are physical units such as consultation time, number of sessions, equipment used and materials consumed. These data will be collected using a specific form. In this phase, the prospective method of quantification of resources will be used which, according to literature,³⁷ is a method that collects information on resources according to a prior plan, in conjunction with the clinical study. The consumption is recorded as the actions occur. The resources will be assigned a value and the cost of each treatment determined for each participant and in each group studied, from the first visit to the start of the treatment until the last follow-up visit.

Organisation and statistical treatment of the data

The numerical data are described by means and SDs or medians and IQRs when the distribution is not presented as normal. The categorical variables are described by means of absolute frequencies and percentages. The measure of outcome used in this study will be the cost ratio and the effectiveness evaluated by muscle pain reported by the patient.

Measurement of costs: monetary units (C)

Measurement of effects (effectiveness): PAIN

Treatment groups: G1 (photobiomodulation), G2 (occlusal splint) and G3 (placebo)

Analyses: $(C_{G1}/PAIN_{G1}) - (C_{G2}/PAIN_{G2})$

CE (cost-effectiveness) = $(C_{G1} - C_{G2}) / (PAIN_{G1} - PAIN_{G2})$

The data will be tabulated and processed using SPSS V.21.0 for Windows. Descriptive statistics will be used for presentation of the distribution of the variables. To evaluate the association of categorical variables, the χ^2 and Fisher's exact tests will be used; for the comparison of means, the Student's t-test and analysis of variance will be used; and for the correlation analysis between continuous variables, Pearson's correlation test will be applied. If subjects fail to report at a follow-up, we will use an ITT analysis. A t-test will be performed to compare the changes in measures within groups. A significance level of 95% ($p < 0.05$) will be considered.

The study will follow the flow chart presented in figure 1.

DISCUSSION

TMD is the most common orofacial pain and myogenic TMD is frequently the subtype. As TMD can be self-limiting, and the patients present with pain, loss of function

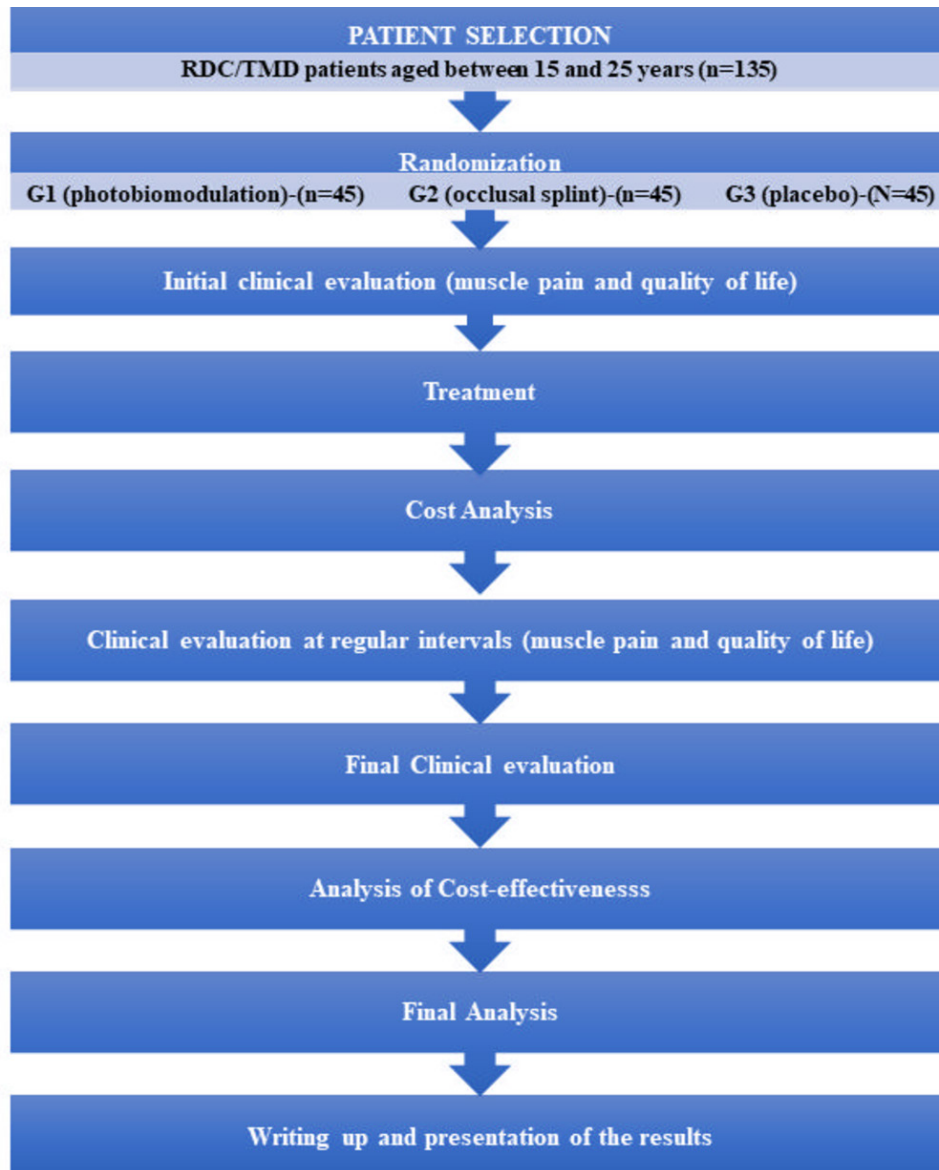


Figure 1 Flow chart of the search strategy. RDC/TMD, Research Diagnostic Criteria for Temporomandibular Disorders.

and trismus, TMD affects the quality of life.^{38–40} Due to this, it is very important to know which treatment (occlusal splint or photobiomodulation therapy) is more cost-effective for TMD pain.

Therapy with an occlusal splint is commonly used as the basic TMD treatment in dental practice, because it is simple to manufacture, low cost and reversible, and gives more efficient results for the treatment of the most painful symptoms of TMD.^{32,41}

Photobiomodulation therapy has been used to control pain in TMD and clinical studies have reported favourable results.^{4–7, 16–24, 26} However, the relationship between the cost of treatment and its effectiveness has not been established in the literature. Clinical and economic data evaluated together can serve as a support for decision-making in choosing a treatment or a new protocol to provide optimum conditions for affected patients.

TMD has a multifactorial aetiology and complex dysfunction, so, the goal of this study is to evaluate the control of chronic pain of the myofascial muscles in each of the groups analysed, and not to treat TMD.

Cost-effectiveness analysis has been used when costs are a crucial factor when choosing a certain product or technology. It has been considered the most suitable method of comparing two or more alternatives of a new technology in health. Thus, in health, economic analysis represents the evaluation of alternative choices for allocation of resources. It has great importance, since it evaluates and compares alternatives and facilitates the use and proper allocation of resources to spheres that may have greater benefits regarding reduction of morbidity costs or greater clinical effect.⁴²

The development of a clinical and economic trial for control of muscle pain in patients with TMD provides

relevant information for clinical decision-making and choosing new care protocols for inclusion. Through this study, we hope to obtain: data related to the direct costs of treatments with photobiomodulation therapy and occlusal splints in the treatment of muscle pain in patients with TMD; determine the ratio between the cost and effectiveness of treatments, considering pain as the end point for measuring effectiveness; and define the impact of the treatments evaluated on the quality of life of patients with TMD.

Contributors Substantial contributions to the conception: APTS and LJM. Design of the work: CLHdG, APTS and LJM. Drafting the work: APTS and LJM. Revising the work: APTS, CLHdG, KPSF, SKB, RAMF, ACRTH, SFM and LJM. Final approval of the work: SKB, KPSF, APTS and LJM.

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Patient consent Obtained.

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