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EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS: A STUDY PROTOCOL FOR A RANDOMIZED CLINICAL TRIAL

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-054523
Article Type:	Protocol
Date Submitted by the Author:	15-Jun-2021
Complete List of Authors:	Shindova, Maria; Medicinski universitet-Plovdiv, Department of Paediatric Dentistry Belcheva, Ani; Medicinski universitet-Plovdiv, Department of Pediatric Dentistry
Keywords:	Paediatric anaesthesia < ANAESTHETICS, Laser therapy < DERMATOLOGY, Child & adolescent psychiatry < PSYCHIATRY, Anxiety disorders < PSYCHIATRY

EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS: A STUDY PROTOCOL FOR A RANDOMIZED CLINICAL TRIAL

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Abstract

Introduction

When providing dental care to children with a high level of dental anxiety, the range of approaches are divided into two sections – use of behavior management techniques and application of alternative methods for caries removal. In an attempt to reduce dental anxiety, they can be mixed and matched in accordance with the dentists` choice. Owing to the promoted advantages Er:YAG laser turns into an ideal alternative technique for hard dental tissue therapy in anxious pediatric

patients. The aim of the study is to assess the efficacy of a modified version of the behavior management technique Latent inhibition in combination with Er:YAG laser for achieving reduction of dental anxiety in pediatric dental patients.

Methods and analysis

This is a protocol for a randomized controlled clinical trial. The participants will be children aged 6-12 years, requiring conservative treatment of occlusal carious lesion on a second primary molar. Patients will be randomly assigned to the experimental or control group via a computer-generated sequence. In both groups, Latent inhibition will be used as an anxiety-management technique. In the experimental group caries treatment will be performed with Erbium:YAG laser, whereas in the control group with the conventional rotary instruments. Outcome measures will be dental anxiety felt before and after the treatment, reported by the patient on a modified version of Faces Scale by LeBaron and the dynamics of heart rate, registered during the treatment session, measured with a mobile pulse oximeter. Data will be analyzed by Independent sample t-test and paired t-test, $p<0.05$.

Ethics and dissemination

The study protocol has been approved by the Committee for Scientific Research Ethics, Medical University-Plovdiv, Bulgaria (Reference number P-2839, Protocol of approval No. 3/30.04.2015) and registered on a publicly accessible database. This research received institutional funding from the Medical University–Plovdiv, Bulgaria. The results will be presented through peer-reviewed publications and conference presentations.

Trial registration: ClinicalTrials.gov (Registration number: NCT04924452).

Keywords: Er:YAG laser, anxiety, management technique, pediatric dentistry

Article Summary

Strengths and limitations of this study

- The study focuses on the implementation of known behavior management technique in the alternative caries treatment method resulting in a reduction of dental anxiety in pediatric dental patients.

- This is the first trial to study the efficacy of Er:YAG laser therapy in combination with a behavior management technique in reducing anxiety among pediatric dental patients.
- A key strength of this study is that all participants meeting eligibility criteria will receive active treatment.
- Both subjective and objective tools are used to assess dental anxiety in this study.
- A limitation of this study is that it is not a split-mouth design whose advantage is the reduction of the outcome variability estimation, leading to the potential increase in statistical power.

1. Introduction

1.1. Background and rationale

When providing dental care to children with a high level of dental anxiety, most pediatric dentists find the conventional rotary treatment method inefficient and uncomfortable. According to the principles of behavioral dentistry, as part of pediatric postgraduate education, the so-called `4S` principle must be adapted and modified to the individual clinical situation to provide adequate dental care to anxious pediatric patients [1]. The range of approaches can be divided into two sections – behavior management techniques (BMTs), on one hand, and alternative methods for caries removal, on the other hand. In an attempt to reduce dental anxiety, they can be mixed and matched in accordance with the dentists` choice.

As it has been found for more than 20 years that lasers are effective for caries excavation, Laser pediatric dentistry has been rapidly developed. It offers total innovation and changes the conventional restorative treatment in pedodontics [2]. Owing to the promoted advantages such as minimal intervention and prevention, safety due to the low penetration depth of the laser beam, selective removal of caries lesion, lack of thermal damage, no pain perception and use of local anesthesia, a significant decrease of patient discomfort and dental anxiety and increase of subjective acceptance and tolerance of laser therapy in children, Er:YAG laser turns into an ideal laser for hard dental tissue therapy in anxious pediatric patients [2,3,4].

Based on the concepts of Minimal Invasive Dentistry (MID), the use of BMTs during the treatment of anxious children to reduce their anxiety is required [5]. Several specific BMTs are not part of the regular curricula of dental students and have been used by pediatric dentists only[4,6,7]. Such a phycological technique is Latent inhibition also known as Gradual exposure [8,9]. It involves a series of several positive non-painful – check-ups and preventive procedures, before any invasive or

painful dental manipulations. Step by step the child is exposed to potential anxiety-provoking procedures or instruments, resulting in an acquaintance with the dental setting and personnel, as well as being accustomed to dental treatment. Despite the specific indications, required preparation and higher time consumption, the use of this technique is very rewarding as the pediatric patient eventually becomes comfortable with the dental procedure and creates a feeling of ability to cope within the child [6,7,10].

Over the recent years, dentists advance in using alternative methods for caries removal as part of their everyday practice. Therefore, the investigation of this synergetic effect of laser caries removal and the different BMTs is crucial for the present and future development of pediatric dentistry and will improve the quality of dental care.

1.2. Objectives

The aim of the study is to assess the efficacy of a modified version of the BMT Latent inhibition in combination with Er:YAG laser for achieving a reduction of dental anxiety in paediatric dental patients. The main objectives are to compare dental anxiety felt during the laser and conventional dental treatment. The outcomes will be dental anxiety assessment by self-reported anxiety scale during treatment in both groups as well as the measurement of heart rate dynamics during the procedures.

1.3. Trial design

The research is designed as a randomized parallel-group controlled clinical study. Table 1 presents the recruiting, allocation, interventions, monitoring, and analysis of the research in accordance with the Standard Protocol Items: Recommendations for Interventional Trials recommendations[11]. In accordance with the Latent inhibition technique patients will have two visits to the dental office – a preventive procedure, the first one, and treatment of caries lesion, the second one. Two groups will be compared. In the experimental group the enamel conditioning of the occlusal surfaces of the permanent molars before sealant application as well as the standardized caries treatment will be performed with Erbium:YAG laser, whereas in the control group the conventional rotary instruments - high-speed and low-speed dental handpieces, will be used for the caries treatment.

Table 1. Trial design. The table summarises the enrolment, allocation, interventions, and assessments in the trail

	STUDY PERIOD				
	Enrolment	**Allocation**	**Post-allocation**		
TIMEPOINT*	**$-t_1$**	**0**	**t_1**	**t_2**	**t_3**
ENROLMENT					
Eligibility screening	×				
Informed consent	×				
Allocation		×			
INTERVENTIONS					
Experimental group (BMT + Laser treatment of dental caries)				×	
Control group (BMT + Caries treatment with conventional rotary instruments)				×	
ASSESSMENTS					
Self-reported dental anxiety			×		×
Heart rate			←	—	→

*Post-allocation time frame: t1 - before the start of the treatment; t_2 - during laser or conventional treatment; t_3 – end of the treatment, before leaving the dental chair.

2. Methods and analyses

2.1. Study setting

The study setting of this research includes the Department of Paediatric Dentistry and the Laser Centre of the Faculty of Dental medicine, Medical University – Plovdiv, Bulgaria.

2.2. Eligibility

2.2.1. Inclusion criteria

1. Participants in the study are children aged 6-12 years, compliant with the cognitive development of the child;
2. Children, requiring conservative treatment of occlusal carious lesions on a second primary molar, without spontaneous unprovoked pain, percussion or palpation pain or other symptoms, indicating pulp involvement or periodontal pathology. Lesions are classified as a distinct cavity with visible dentin without prior restoration or sealants by the International Caries Detection and Assessment System (ICDAS) with code 05 [12,13,14]. Included are caries lesions only on vital teeth.
3. Children with one or more permanent molars giving indications for pit and fissure sealing;
4. Patients without previous experience with laser treatment of carious lesions;
5. Children who are not considered medically compromised or medically complex patients;
6. Verbal assent from the child willing to comply with all study procedures and protocol;
7. Obtained written informed consent by the patient`s parent/guardian for participation in the study (see supplementary data file S1 `Patient consent form` and S2 `Information leaflet`).

2.2.2. Exclusion criteria

1. Patients who were undergoing therapy with neurological, sedative, analgesic, and/or anti-inflammatory drugs 7 days prior to treatment that might affect heart rate;
2. Children, who were first-time dental patients;
3. Children with systemic diseases or physiological development delays;
4. Children with mental or cognitive problems;
5. Active infectious diseases such as influenza, scarlet fever, etc.
6. Excluded are molars which are affected by disturbances in the development of dental structures (hypoplasia, hypomineralization, fluorosis)

2.2.3. Interventions

Patients will be divided into 2 groups (41 per group) – experimental and control groups. All treatments will be carried out by the same operator (MS), without anesthesia. A baseline dental self-reported anxiety will be recorded using a Faces anxiety scale as well as the dynamics of heart rate, measured with a mobile pulse oximeter.

Er:YAG laser therapy protocol (experimental group):

Er:YAG laser (LiteTouch, Light Instruments LTD), emission wavelength 2940 nm will be used for enamel conditioning of the occlusal surfaces of the permanent molars before sealant application as well as the standardized caries treatment. Chosen protocol parameters are modified based on previously conducted studies [2,3,4,15,16]:

- preventive procedure – sealant application:

- a low-speed rubber cup and pumice paste (CleanPolish, Kerr) will be used for 30 seconds for cleaning and polishing of the occlusal surface of the chosen permanent molar;
- tooth surface will be washed for debris and organic residue removal and dried with air spray;
- isolation;
- laser conditioning of the occlusal enamel surface. The parameter settings used will be: tip-to-tissue distance 1.5mm from the tooth surface; tip diameter 600 μm; laser energy 70 mJ; pulse frequency 10 Hz; water spray level 8; average power 0.7 W; energy density 67 J/cm^2;
- tooth surface will be etched with 35% phosphoric acid gel (Etching gel, DMP Ltd) for 30 seconds and rinsed for the same time;
- reisolation;
- tooth surface will be dried with air spray for 15s;
- fissure sealant application (Pit&Fisssure Sealant, DMP Ltd);
- light cured for 20 seconds.

- caries removal – parameters: enamel removal – energy 100-200mJ; density 9.84-13.03 J/cm^2, pulse frequency 20Hz; tip diameter 800 μm; water spray level 8; tip-to-tissue distance 0.5÷1 mm from the tooth surface; dentin removal - energy 100mJ; density 9.84 J/cm^2, pulse frequency 20Hz; tip diameter 800 μm; water spray level 8; tip-to-tissue distance 0.5÷1 mm form the tooth surface. Restoration with compomer.

Conventional therapy protocol (control group):

- preventive procedure – sealant application

- a low-speed rubber cup and pumice paste (CleanPolish, Kerr) will be used for 30 seconds for cleaning and polishing of the occlusal surface of the chosen permanent molar;
- tooth surface will be washed for debris and organic residue removal and dried with air spray;

- isolation;
- tooth surface will be etched with 35% phosphoric acid gel (Etching gel, DMP Ltd) for 30 seconds and rinsed for the same time;
- reisolation;
- tooth surface will be dried with air spray for 15s;
- fissure sealant application (Pit&Fisssure Sealant, DMP Ltd);
- light cured for 20 seconds.

- caries removal – conventional rotary instruments will be used - high-speed and low-speed dental handpieces. Restoration with compomer.

2.2.4. Clinical protocol

First visit:

1. Parents/guardians are informed about the protocol of the study and the laser technique. They sign the informed consent form (see Supplementary data files S1 and S2). Verbal assent from the child is obtained.
2. Oral examination and sealant application are performed according to the assigned intervention.
3. Patient`s self-report of dental anxiety before leaving the dental chair.

Second visit:

1. Patients will be asked to report their dental anxiety, pointing to the face or choose the number which most closely depicted its state of anxiety using a modified version of the self-report Faces Scale by LeBaron et al.[17] (see Supplementary data file S3)
2. Pulse-oximeter is connected to the patient`s index finger. The start of heart rate monitoring and recording will be 5 minutes prior to treatment. Time frame: at least 5 minutes after the dental treatment, before leaving the dental chair.
3. Caries treatment is performed according to the assigned intervention.
4. Patient`s self-report of dental anxiety before leaving the dental chair.

2.3. Outcomes

2.3.1. Primary outcome measures

The primary outcome measures will be the dental anxiety felt, reported by the patient on a modified version of the self-report Faces Scale by LeBaron et al. before and after the treatment session. The scale comprises a row of five faces ranging from `relaxed` to `very worried` in combination with a

visual analog scale of 0 – 10. Each child was asked to point to the face or choose the number which most closely depicted its state of anxiety.

2.3.2. Secondary outcome measures

The secondary outcome measures will be the dynamics of heart rate, registered during the treatment session measured with a mobile pulse oximeter (CMS50F, CONTEC), placed on the index finger of the left hand [18]. Throughout the whole procedure of each dental visit, data were recorded and analyzed by a specially developed digital processing and graphic visualization software SPO2 Review V1.2 rel.

2.3.3. Participant`s timeline

Each eligible patient undergoes two visits. The first appointment includes screening, consenting and assenting, recording of dental anxiety, sealant application according to the assigned interventions for each group. The second appointment at the one-week recall includes a recording of dental anxiety and treatment of a carious lesion according to the assigned interventions for each group. The manipulations will be performed by one operator.

2.3.4. Sample size calculation

The sample size calculation is performed based on data from a pilot study with 20 subjects. The sample size is calculated to assure a test power greater than 95% and a significant level of $\alpha = 0.05$. We estimated a sample size of 41 patients per group to detect significant differences. Thus, the final sample size for this study will be 82 patients.

2.4. Recruitment

The patients at the Department of Paediatric Dentistry of the Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria, who meet the inclusion criteria, will be screened for eligibility. Once identified, patients will be informed about this research project and will receive information about the possibility of potential study participation. Patient recruitment starts obtaining the full quota of participants within a one-year time frame. It begins in September 2021 with an estimated enrollment capacity of 5 patients per month.

2.5. Participating centers

The patients are randomly selected from the visitors in the Department of Paediatric Dentistry of the Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria, and treated in the Laser Centre of the same university.

2.6. Assignment of the intervention

2.6.1. Sequence generation

The patients will be randomly allocated to either the control group or the experimental group (41 patients in each group) according to the enrolment number in the trial. The randomization will be created using a computerized random generator.

2.6.2. Allocation concealment mechanism and implementation

A randomization list will be created by a random generator before the start of the treatment and kept in a locked drawer. Assignments will be kept in separate, closed opaque, sequentially numbered envelopes, enabling the sequence to be concealed until the intervention is assigned.

2.6.3. Blinding

The randomisation will be independent, that is, the patients and parents/guardians will remain blinded to group status. The operator will get acquainted with the procedure to be performed prior to the first session. The operator is selected to be the only one performing the manipulation to prevent bias. The statistician will be blinded to treatment assignment as data will be masked before the analysis without giving the statistician the key.

2.6.4. Data collection, confidentiality, storage, and monitoring of the study documents

Collection, coding, storage, and evaluation of personal data within the project will be carried out in accordance with The General Data Protection Regulation (EU) 2016/679 (*GDPR*). A prerequisite for data collection will be the voluntary written informed consent of the patient`s parent or guardian. Confidentiality will be guaranteed by a coded ID number, access will be granted exclusively to the study investigators. The information from the paper forms will be exported to a database file and stored on a password-protected computer. Only the investigators and statistician will have access to the final data set. All data collected will be stored in sealed containers in areas

of the Department of Paediatric Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria with limited access.

3. Statistical methods

The obtained data will be recorded, tabulated, processed, and analyzed using SPSS (Statistical Package for Social Science software) version 21.0 (IBM, USA). In all tests, the significance level of 5% probability or the corresponding *P*-value will be adopted. Descriptive statistics will be calculated. Discrete variables will be summarised by frequencies or proportions. Continuous variables will be presented as means and standard deviations. We will compare anxiety mean scores according to the Faces Scale by LeBaron as well as heart rate mean score. Comparisons among groups will be performed by using the Independent sample t-test and paired t-test.

4. Patient and public involvement

The development of the research question and outcome measures will be based on the review of available evidence in this research area. Patients will not be involved in the development of the study protocol. However, their questions and concerns will be addressed during patient recruitment and study implementation. During the conduction of the study, patients will not be informed about the results of the ongoing trial since there is no planned interim analysis. The results will be disseminated to the study participants through email and routine follow-up dental check-ups.

5. Ethics and dissemination

The clinical study will be conducted in accordance with the conditions and principles of the Declaration of Helsinki, the existing EU Clinical Trial Directive (EC) No. 2001/20/EC, the recommendations of the Ethical Committee at the Medical University of Plovdiv, Bulgaria and the international ethical and scientific quality standard for designing, recording and reporting trials that involve the participation of human subjects - Good Clinical Practices (GCP).

5.1. Research ethics approval

The study was approved by the Committee for Scientific Research Ethics, Medical University - Plovdiv, Bulgaria (Reference number P-2839, Protocol of approval No.3/30.04.2015) and registered on a publicly accessible database ClinicalTrials.gov (Registration number: NCT04924452). Ethical approval for the study protocol and the written informed consent for all

subjects` parents/guardians was granted by the Ethics Committee of the Medical University, Plovdiv, Bulgaria.

5.2. Consent

The operators will obtain written consent from patients` parents/guardians willing to participate in the trial. Additional information will be provided for all parents for the study. Completed informed consent will be collected at the Department of Pediatric Dentistry, Medical University - Plovdiv by the study investigators. A copy of the signed consent form will be handed over to the participating child`s parent/guardian. After providing age-appropriate information about the study, verbal assent will be obtained as an affirmative agreement for participation from children

5.3. Confidentiality

The information of the participants collected during the study will be kept strictly confidential and will not be disclosed to third parties. Confidentiality will be guaranteed by a coded ID number, access will be granted exclusively to the study investigators.

5.4. Conflict of interests

The investigators have no conflicts of interest to declare. They agree with the protocol and the informed consent of the study and there is no financial interest to report.

5.5. Access to data

All data collected will be stored in sealed containers in areas of the Department of Paediatric Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria with limited access. The information from the paper forms will be exported to a database file and stored on a password-protected computer. Only the investigators and statistician will have access to the final data set.

5.6. Dissemination policy

The results of the trial will be presented through peer-reviewed publications and conference presentations. In addition, our results will be disseminated to clinicians, as well as key stakeholders, including scientific directors of postgraduate programs "Master of Science in Lasers in Dentistry", academic courses in Pedodontics and Preventive dentistry. The principle investigator (MS) and the

scientific expert (AB) will write the first draft of the manuscript without the use of professional writers.

Conclusion

The study outlined in this protocol will be the first investigated combination of the treatment effect of the Er:YAG-laser irradiation in addition to a behavior management technique. The implementation of Er:YAG-laser in the regular protocol for behavior guidance during dental treatment would significantly increase the success of this therapy resulting in lower levels of dental anxiety among pediatric dental patients.

As the literature offers no studies reporting the effectiveness of combined use of laser therapy and behavior management techniques in pediatric dentistry, there is an evident need for studies that address these outcomes, since dentists advance in using alternative methods for caries removal as part of their everyday practice.

Trial status

The trial is not yet recruiting patients. The process will start in September 2021 and will continue untill September 2022.

Word count: 3705

Acknowledgements

The authors would like to show their gratitude to Assoc. Prof. Georgi Tomov, PhD for the fruitful discussion. Assistance with the Laser Center of the Faculty of Dental Medicine, Medical University of Plovdiv, Bulgaria was greatly appreciated. The authors are also thankful to Prof. Nonka Mateva, PhD for the statistical consultancy expertise in the planning of this clinical trial.

Author Contributions

We declare that all authors have made substantial contributions. MS and AB conceive the ideas. AB trained MS. MS will be the primary operator, outcomes assessor, and data collector. All authors will participate in the analysis and reporting of the results. Writing will be led by MS. The design and protocol for this study were developed by AB and MS. All authors contributed to refining the study protocol and approving the final manuscript.

Funding

This research received institutional funding from the Medical University – Plovdiv, Bulgaria.

Competing interests

None declared.

Patient consent for publication

(see Supplementary data file S1 `Patient consent form`)

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Consent form

For a patient's consent to publication of images and/or information about them in BMJ publications.

Name of patient:	______________________________
Patient`s parent/guardian:	______________________________
Material – text (information about your child`s oral health, level of dental anxiety and dynamics of heart rate):	______________________________
Provisional title of article in which Material will be included:	Efficacy of Combined Er:YAG Laser Therapy and Behaviour Management Technique in Reducing Anxiety among Paediatric Dental Patients ______________________________

CONSENT

I_______________________________________[ENTER YOUR FULL NAME] give my consent for the Material about my child to appear in a BMJ publication.

I confirm that I: *(please tick boxes to confirm)*

- ☐ ***have seen the text or other material about my child***
- ☐ ***have read the article to be submitted to BMJ***
- ☐ ***am legally entitled to give this consent.***

I understand the following:

(1) The Material will be published without my child`s name attached, however I understand that complete anonymity cannot be guaranteed. It is possible that somebody somewhere may recognise my child.

(2) The Material may show or include details of my child's medical condition or injury and any prognosis, treatment or surgery that I have/the patient has, had or may have in the future.

(3) The article may be published in a journal which is distributed worldwide. BMJ's publications go mainly to doctors and other healthcare professionals but are also seen by many others including academics, students and journalists.

(4) The article, including the Material, may be the subject of a press release, and may be linked to from social media and/or used in other promotional activities. Once published, the article will be placed on a BMJ website and may also be available on other websites.

(5) The text of the article will be edited for style, grammar and consistency before publication.

(6) I and my child will not receive any financial benefit from publication of the article.

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(7) The article may also be used in full or in part in other publications and products published by BMJ and/or by other publishers. This includes publication in English and in translation, in print, in digital formats, and in any other formats that may be used by BMJ or other publishers now and in the future. The article may appear in local editions of journals or other publications, published in the UK and overseas.

(8) I can revoke my consent at any time before publication, but once the article has been committed to publication ("gone to press") it will not be possible to revoke the consent.

(9) This consent form will be retained securely and in confidence by BMJ in accordance with the law, for no longer than necessary. Personal data provided in this form will be used and retained in accordance with BMJ's Privacy Policy available at https://www.bmj.com/company/your-privacy/.

Signed: ______________________ *Print name:* ______________________

Address: ______________________ *Email address:* ______________________

______________________ *Telephone no:* ______________________

** signing on behalf of the patient who is under the age of 18*

______________________ *Date:* ______________________

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Date: ______________________

Patient consent form 050419

INFORMATION LEAFLET

DEPARTMENT OF PAEDIATRIC DENTISTRY
LASER CENTER
FACULTY OF DENTAL MEDICINE,
MEDICAL UNIVERSITY OF PLOVDIV, BULGARIA

EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS

DESCRIPTION: You and your child are invited to participate in a research study on the efficiency of Er:YAG laser therapy in combination with behavior management technique in reducing anxiety among pediatric dental patients.

PROCEDURES: With your permission, we would like to collect information about your children`s dental anxiety before, during and after dental treatment of a caries lesion. This study does not involve any experiments, just preventive procedures and dental treatment, collection, and study of the required information.

RISKS AND BENEFITS: There are no anticipated risks associated with this study. You will not receive any direct benefit from participation.

TIME INVOLVEMENT: Your child`s participation in this study will not require more time from you other than for the first visit including an explanation of the study, oral examination and a preventive procedure (sealant application). The second appointment at 7-day recall will include dental treatment.

PAYMENTS: You will not be paid to participate in this study. You will not pay for the treatment of your child in this study.

PARTICIPANT'S RIGHTS: If you have read this form and have decided your child to participate in this research, please understand your participation is voluntary and you have the right to withdraw your consent or discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

The results of this research study may be presented at scientific or professional meetings or published in scientific journals. However, your identity will not be disclosed**.**

Thank you for your time and attention!

Name of parent/guardian .....

Signature of parent /guardian .....

Name of patient .....

Telephone number .....

Name of the dentist .....

Signature of the dentist .....

For additional information regarding the trial, you can contact us at the given address, emails, or phone numbers.

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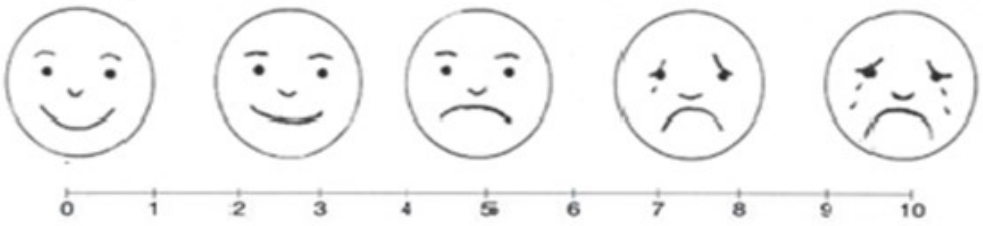

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Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	2,14
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	2
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3,4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3,4
Objectives	#7	Specific objectives or hypotheses	4

Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	4
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5,6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5,6
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	n/a
Interventions:	#11c	Strategies to improve adherence to intervention protocols,	n/a

adherance		and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests) Non-adherence interventions in the present study	
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial No permitted or prohibited during the trial concomitant care and interventions	n/a
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8,9
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Table 1)	9
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
Recruitment	#15	Strategies for achieving adequate participant enrolment to	9

		reach target sample size	
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a

		open-label trial	
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10,11
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10,11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11

Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	n/a
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			

Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11,12
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	11,12
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	12
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	12
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	12
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial	n/a

		participation	
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12,13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	12
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Suppl 1-3
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

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EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS: A STUDY PROTOCOL FOR A RANDOMIZED CLINICAL TRIAL

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-054523.R1
Article Type:	Protocol
Date Submitted by the Author:	13-Dec-2021
Complete List of Authors:	Belcheva, Ani; Medicinski universitet-Plovdiv, Department of Paediatric Dentistry Shindova, Maria; Medicinski universitet-Plovdiv, Department of Paediatric Dentistry
Primary Subject Heading:	Dentistry and oral medicine
Secondary Subject Heading:	Dentistry and oral medicine
Keywords:	Paediatric anaesthesia < ANAESTHETICS, Laser therapy < DERMATOLOGY, Child & adolescent psychiatry < PSYCHIATRY, Anxiety disorders < PSYCHIATRY

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Abstract

Introduction

When providing dental care to children with a high level of dental anxiety, the range of approaches are divided into two sections – use of behavior management techniques and application of alternative methods for caries removal. In an attempt to reduce dental anxiety, they can be mixed and matched in accordance with the dentists` choice. Owing to the promoted advantages Er:YAG laser turns into an ideal alternative technique for hard dental tissue therapy in anxious pediatric

patients. The aim of the study is to assess the efficacy of a modified version of the behavior management technique Latent inhibition in combination with Er:YAG laser for achieving a reduction of dental anxiety in pediatric dental patients.

Methods and analysis

This is a protocol for a randomized controlled clinical trial. The participants will be children aged 6-9 years, requiring conservative treatment of occlusal carious lesion on a second primary molar. Patients will be randomly assigned to the experimental or control group via a computer-generated sequence. In both groups, Latent inhibition will be used as an anxiety-management technique. In the experimental group caries treatment will be performed with Erbium:YAG laser, whereas in the control group with the conventional rotary instruments. Outcome measures will be dental anxiety felt before and after the treatment, reported by the patient on a modified version of Faces Scale by LeBaron and the dynamics of heart rate, registered during the treatment session, measured with a mobile pulse oximeter. Data will be analyzed by Independent sample t-test and paired t-test, $p<0.05$.

Ethics and dissemination

The study protocol has been approved by the Committee for Scientific Research Ethics, Medical University-Plovdiv, Bulgaria (Reference number P-2839, Protocol of approval No. 3/30.04.2015) and registered on a publicly accessible database. This research received institutional funding from the Medical University–Plovdiv, Bulgaria. The results will be presented through peer-reviewed publications and conference presentations.

Trial registration: ClinicalTrials.gov (Registration number: NCT04924452).

Keywords: Er:YAG laser, anxiety, management technique, pediatric dentistry

Article Summary

Strengths and limitations of this study

- The study focuses on the implementation of a known behavior management technique in the alternative caries treatment method resulting in a reduction of dental anxiety in pediatric dental patients.

- This is the first trial to study the efficacy of Er:YAG laser therapy in combination with a behavior management technique in reducing anxiety among pediatric dental patients.
- A key strength of this study is that all participants meeting eligibility criteria will receive active treatment.
- Both subjective and objective tools are used to assess dental anxiety in this study.
- A limitation of this study is that it is not a split-mouth design whose advantage is the reduction of the outcome variability estimation, leading to the potential increase in statistical power.

1. Introduction

1.1. Background and rationale

When providing dental care to children with a high level of dental anxiety, most pediatric dentists find the conventional rotary treatment method inefficient and uncomfortable. According to the principles of behavioral dentistry, as part of pediatric postgraduate education, the so-called `4S` principle must be adapted and modified to the individual clinical situation to provide adequate dental care to anxious pediatric patients [1]. The range of approaches can be divided into two sections – behavior management techniques (BMTs), on one hand, and alternative methods for caries removal, on the other hand. In an attempt to reduce dental anxiety, they can be mixed and matched in accordance with the dentists` choice.

As it has been found for more than 20 years that lasers are effective for caries excavation, Laser pediatric dentistry has been rapidly developed. It offers total innovation and changes the conventional restorative treatment in pedodontics [2]. Owing to the promoted advantages such as minimal intervention and prevention, safety due to the low penetration depth of the laser beam, selective removal of caries lesion, lack of thermal damage, no pain perception and use of local anesthesia, a significant decrease of patient discomfort and dental anxiety and increase of subjective acceptance and tolerance of laser therapy in children, Er:YAG laser turns into an ideal laser for hard dental tissue therapy in anxious pediatric patients [2,3,4].

Based on the concepts of Minimal Invasive Dentistry (MID), the use of BMTs during the treatment of anxious children to reduce their anxiety is required [5]. Several specific BMTs are not part of the regular curricula of dental students and have been used by pediatric dentists only[4,6,7]. Such a phycological technique is Latent inhibition also known as Gradual exposure [8,9]. It involves a series of several positive non-painful – check-ups and preventive procedures, before any invasive or

painful dental manipulations. Step by step the child is exposed to potential anxiety-provoking procedures or instruments, resulting in an acquaintance with the dental setting and personnel, as well as being accustomed to dental treatment. Despite the specific indications, required preparation and higher time consumption, the use of this technique is very rewarding as the pediatric patient eventually becomes comfortable with the dental procedure and creates a feeling of ability to cope within the child [6,7,10].

Over the recent years, dentists advance in using alternative methods for caries removal as part of their everyday practice. Therefore, the investigation of this synergetic effect of laser caries removal and the different BMTs is crucial for the present and future development of pediatric dentistry and will improve the quality of dental care.

1.2. Objectives

The aim of the study is to assess the efficacy of a modified version of the BMT Latent inhibition in combination with Er:YAG laser for achieving a reduction of dental anxiety in paediatric dental patients. The main objectives are to compare dental anxiety felt during the laser and conventional dental treatment. The outcomes will be dental anxiety assessment by self-reported anxiety scale during treatment in both groups as well as the measurement of heart rate dynamics during the procedures.

1.3. Trial design

The research is designed as a randomized parallel-group controlled clinical study. Table 1 presents the recruiting, allocation, interventions, monitoring, and analysis of the research in accordance with the Standard Protocol Items: Recommendations for Interventional Trials recommendations[11]. In accordance with the Latent inhibition technique patients will have two visits to the dental office – a preventive procedure, the first one, and treatment of caries lesion, the second one. Two groups will be compared. In the experimental group the enamel conditioning of the occlusal surfaces of the permanent molars before sealant application as well as the standardized caries treatment will be performed with Erbium:YAG laser, whereas in the control group the conventional rotary instruments - high-speed and low-speed dental handpieces, will be used for the caries treatment.

Table 1. Trial design. The table summarises the enrolment, allocation, interventions, and assessments in the trail

	STUDY PERIOD				
	Enrolment	**Allocation**	**Post-allocation**		
TIMEPOINT*	**$-t_1$**	**0**	**t_1**	**t_2**	**t_3**
ENROLMENT					
Eligibility screening	×				
Informed consent	×				
Allocation		×			
INTERVENTIONS					
Experimental group (BMT + Laser treatment of dental caries)				×	
Control group (BMT + Caries treatment with conventional rotary instruments)				×	
ASSESSMENTS					
Self-reported dental anxiety			×		×
Heart rate			←	—	→

*Post-allocation time frame: t1 - before the start of the treatment; t_2 - during laser or conventional treatment; t_3 – end of the treatment, before leaving the dental chair.

2. Methods and analyses

2.1. Study setting

The study setting of this research includes the Department of Paediatric Dentistry and the Laser Centre of the Faculty of Dental medicine, Medical University – Plovdiv, Bulgaria.

2.2. Eligibility

2.2.1. Inclusion criteria

1. Participants in the study are children aged 6-9 years, compliant with the cognitive development of the child;
2. Children, requiring conservative treatment of occlusal carious lesions on a second primary molar, without spontaneous unprovoked pain, percussion or palpation pain or other symptoms, indicating pulp involvement or periodontal pathology. Lesions are classified as a distinct cavity with visible dentin without prior restoration or sealants by the International Caries Detection and Assessment System (ICDAS) with code 05 [12,13,14]. Included are caries lesions only on vital teeth.
3. Children with one or more permanent molars giving indications for pit and fissure sealing;
4. Patients without previous experience with laser treatment of carious lesions;
5. Children who are not considered medically compromised or medically complex patients;
6. Verbal assent from the child willing to comply with all study procedures and protocol;
7. Obtained written informed consent by the patient`s parent/guardian for participation in the study (see supplementary data file S1 `Patient consent form` and S2 `Information leaflet`).

2.2.2. Exclusion criteria

1. Patients who were undergoing therapy with neurological, sedative, analgesic, and/or anti-inflammatory drugs 7 days prior to treatment that might affect heart rate;
2. Children, who were first-time dental patients;
3. Children with systemic diseases or physiological development delays;
4. Children with mental or cognitive problems;
5. Active infectious diseases such as influenza, scarlet fever, etc.
6. Excluded are molars which are affected by disturbances in the development of dental structures (hypoplasia, hypomineralization, fluorosis)

2.2.3. Interventions

Patients will be divided into 2 groups (41 per group) – experimental and control groups. All treatments will be carried out by the same operator (MS), without anesthesia. A baseline dental self-reported anxiety will be recorded using a Faces anxiety scale as well as the dynamics of heart rate, measured with a mobile pulse oximeter.

Er:YAG laser therapy protocol (experimental group):

Er:YAG laser (LiteTouch, Light Instruments LTD), emission wavelength 2940 nm will be used for enamel conditioning of the occlusal surfaces of the permanent molars before sealant application as well as the standardized caries treatment. Chosen protocol parameters are modified based on previously conducted studies [2,3,4,15,16]:

- preventive procedure – sealant application:

- a low-speed rubber cup and pumice paste (CleanPolish, Kerr) will be used for 30 seconds for cleaning and polishing of the occlusal surface of the chosen permanent molar;
- tooth surface will be washed for debris and organic residue removal and dried with air spray;
- isolation with rubber dam;
- laser conditioning of the occlusal enamel surface. The parameter settings used will be: tip-to-tissue distance 1.5mm from the tooth surface; tip diameter 600 µm; laser energy 70 mJ; pulse frequency 10 Hz; water spray level 8; average power 0.7 W; energy density 67 J/cm^2;
- tooth surface will be etched with 35% phosphoric acid gel (Etching gel, DMP Ltd) for 30 seconds and rinsed for the same time;
- tooth surface will be dried with air spray for 15s;
- fissure sealant application (Pit&Fisssure Sealant, DMP Ltd);
- light cured for 20 seconds.

caries removal – parameters: enamel removal – energy 100-200mJ; density 9.84-13.03 J/cm^2, pulse frequency 20Hz; tip diameter 800 µm; water spray level 8; tip-to-tissue distance 0.5÷1 mm from the tooth surface; dentin removal - energy 100mJ; density 9.84 J/cm^2, pulse frequency 20Hz; tip diameter 800 µm; water spray level 8; tip-to-tissue distance 0.5÷1 mm form the tooth surface. Restoration with compomer. Time for caries removal procedure – max 8 minutes [17,18,19,20].

Conventional therapy protocol (control group):

- preventive procedure – sealant application

- a low-speed rubber cup and pumice paste (CleanPolish, Kerr) will be used for 30 seconds for cleaning and polishing of the occlusal surface of the chosen permanent molar;
- tooth surface will be washed for debris and organic residue removal and dried with air spray;
- isolation with rubber dam;

- tooth surface will be etched with 35% phosphoric acid gel (Etching gel, DMP Ltd) for 30 seconds and rinsed for the same time;
- tooth surface will be dried with air spray for 15s;
- fissure sealant application (Pit&Fisssure Sealant, DMP Ltd);
- light cured for 20 seconds.

- caries removal – conventional rotary instruments will be used - high-speed and low-speed dental handpieces. For the bur preparation 1.2 mm diameter diamond round bur Drendel & Zweiling No. 801.314. and Komet Steel round bur 016, Komet Dental Gebr were used. A new bur was used for each preparation. Restoration with compomer. Time for caries removal procedure – max 4 minutes.

2.2.4. Clinical protocol

First visit:

1. Parents/guardians are informed about the protocol of the study and the laser technique. They sign the informed consent form (see Supplementary data files S1 and S2). Verbal assent from the child is obtained.
2. Oral examination and sealant application are performed according to the assigned intervention.
3. Patient`s self-report of dental anxiety before leaving the dental chair.

Second visit:

1. Patients will be asked to report their dental anxiety, pointing to the face or choose the number which most closely depicted its state of anxiety using a modified version of the self-report Faces Scale by LeBaron et al.[21] (see Supplementary data file S3)
2. Pulse-oximeter is connected to the patient`s index finger. The start of heart rate monitoring and recording will be 5 minutes prior to treatment. Time frame: at least 5 minutes after the dental treatment, before leaving the dental chair.
3. Caries treatment is performed according to the assigned intervention.
4. Patient`s self-report of dental anxiety before leaving the dental chair.

2.3. Outcomes

2.3.1. Primary outcome measures

The primary outcome will be the dental anxiety before and after the treatment session, reported by the patient on a modified version of the self-report Faces Scale by LeBaron et al.. The scale

comprises a row of five faces ranging from `relaxed` to `very worried` in combination with a visual analog scale of 0 – 10. Each child was asked to point to the face or choose the number which most closely depicted its state of anxiety.

2.3.2. Secondary outcome measures

The secondary outcome will be the dynamics of heart rate, registered during the treatment session measured with a mobile pulse oximeter (CMS50F, CONTEC), placed on the index finger of the left hand [22]. Throughout the whole procedure of each dental visit, data were recorded and analyzed by a specially developed digital processing and graphic visualization software SPO2 Review V1.2 rel.

2.3.3. Participant`s timeline

Each eligible patient undergoes two visits. The first appointment includes screening, consenting and assenting, recording of dental anxiety, sealant application according to the assigned interventions for each group. The second appointment at the one-week recall includes a recording of dental anxiety and treatment of a carious lesion according to the assigned interventions for each group. The manipulations will be performed by one operator.

2.3.4. Sample size calculation

The sample size calculation is performed based on data from a pilot study with 20 subjects. To estimate sample size for the primary outcome—self-reported anxiety felt, according to the Faces Scale by LeBaron —a t-test for paired groups has been used (G* Power software V.3.1,6 since we have two groups). The effect size was determined using the formula

$$ES = \frac{Control - Treated}{SDpooled} = \frac{2.33 - 0.33}{3.25} = 0.62$$

where SD is the pooled SD, an average of the SD of the experimental and control groups. The sample size is calculated to assure a test power greater than 95% and a significant level of $\alpha = 0.05$. We estimated a sample size of 41 patients per group to detect significant differences. Thus, the final sample size for this study will be 82 patients.

2.4. Recruitment

The patients at the Department of Paediatric Dentistry of the Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria, who meet the inclusion criteria, will be screened for eligibility.

Once identified, patients will be informed about this research project and will receive information about the possibility of potential study participation. Patient recruitment starts obtaining the full quota of participants within a one-year time frame. It begins in September 2021 with an estimated enrollment capacity of 5 patients per month.

2.5. Participating centers

The patients are randomly selected from the visitors in the Department of Paediatric Dentistry of the Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria, and treated in the Laser Centre of the same university.

2.6. Assignment of the intervention

2.6.1. Sequence generation

The patients will be randomly allocated to either the control group or the experimental group (41 patients in each group) according to the enrolment number in the trial. The randomization will be created using a computerized random generator.

2.6.2. Allocation concealment mechanism and implementation

A randomization list will be created by a random generator before the start of the treatment and kept in a locked drawer. Assignments will be kept in separate, closed opaque, sequentially numbered envelopes, enabling the sequence to be concealed until the intervention is assigned.

2.6.3. Blinding

The randomisation will be independent, that is, the patients and parents/guardians will remain blinded to group status. The operator will get acquainted with the procedure to be performed prior to the first session. The operator is selected to be the only one performing the manipulation to prevent bias. The statistician will be blinded to treatment assignment as data will be masked before the analysis without giving the statistician the key.

2.6.4. Data collection, confidentiality, storage, and monitoring of the study documents

Collection, coding, storage, and evaluation of personal data within the project will be carried out in accordance with The General Data Protection Regulation (EU) 2016/679 (*GDPR*). A prerequisite for data collection will be the voluntary written informed consent of the patient`s

parent or guardian. Confidentiality will be guaranteed by a coded ID number, access will be granted exclusively to the study investigators. The information from the paper forms will be exported to a database file and stored on a password-protected computer. Only the investigators and statistician will have access to the final data set. All data collected will be stored in sealed containers in areas of the Department of Paediatric Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria with limited access.

3. Statistical methods

The obtained data will be recorded, tabulated, processed, and analyzed using SPSS (Statistical Package for Social Science software) version 21.0 (IBM, USA). In all tests, the significance level of 5% probability or the corresponding *P*-value will be adopted. Descriptive statistics will be calculated. Discrete variables will be summarised by frequencies or proportions. Continuous variables will be presented as means and standard deviations. We will compare anxiety mean scores according to the Faces Scale by LeBaron as well as heart rate mean score. Comparisons among groups will be performed by using the Independent sample t-test and paired t-test.

4. Patient and public involvement

The development of the research question and outcome measures will be based on the review of available evidence in this research area. Patients will not be involved in the development of the study protocol. However, their questions and concerns will be addressed during patient recruitment and study implementation. During the conduction of the study, patients will not be informed about the results of the ongoing trial since there is no planned interim analysis. The results will be disseminated to the study participants through email and routine follow-up dental check-ups.

5. Ethics and dissemination

The clinical study will be conducted in accordance with the conditions and principles of the Declaration of Helsinki, the existing EU Clinical Trial Directive (EC) No. 2001/20/EC, the recommendations of the Ethical Committee at the Medical University of Plovdiv, Bulgaria and the international ethical and scientific quality standard for designing, recording and reporting trials that involve the participation of human subjects - Good Clinical Practices (GCP).

5.1. Research ethics approval

The study was approved by the Committee for Scientific Research Ethics, Medical University - Plovdiv, Bulgaria (Reference number P-2839, Protocol of approval No.3/30.04.2015) and registered on a publicly accessible database ClinicalTrials.gov (Registration number: NCT04924452). Ethical approval for the study protocol and the written informed consent for all subjects` parents/guardians was granted by the Ethics Committee of the Medical University, Plovdiv, Bulgaria.

5.2. Consent

The operators will obtain written consent from patients` parents/guardians willing to participate in the trial. Additional information will be provided for all parents for the study. Completed informed consent will be collected at the Department of Pediatric Dentistry, Medical University - Plovdiv by the study investigators. A copy of the signed consent form will be handed over to the participating child`s parent/guardian. After providing age-appropriate information about the study, verbal assent will be obtained as an affirmative agreement for participation from children

5.3. Confidentiality

The information of the participants collected during the study will be kept strictly confidential and will not be disclosed to third parties. Confidentiality will be guaranteed by a coded ID number, access will be granted exclusively to the study investigators.

5.4. Conflict of interests

The investigators have no conflicts of interest to declare. They agree with the protocol and the informed consent of the study and there is no financial interest to report.

5.5. Access to data

All data collected will be stored in sealed containers in areas of the Department of Paediatric Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria with limited access. The information from the paper forms will be exported to a database file and stored on a password-protected computer. Only the investigators and statistician will have access to the final data set.

5.6. Dissemination policy

The results of the trial will be presented through peer-reviewed publications and conference presentations. In addition, our results will be disseminated to clinicians, as well as key stakeholders, including scientific directors of postgraduate programs "Master of Science in Lasers in Dentistry", academic courses in Pedodontics and Preventive dentistry. The principle investigator (MS) and the scientific expert (AB) will write the first draft of the manuscript without the use of professional writers.

Conclusion

The study outlined in this protocol will be the first investigated combination of the treatment effect of the Er:YAG-laser irradiation in addition to a behavior management technique. The implementation of Er:YAG-laser in the regular protocol for behavior guidance during dental treatment would significantly increase the success of this therapy resulting in lower levels of dental anxiety among pediatric dental patients.

As the literature offers no studies reporting the effectiveness of combined use of laser therapy and behavior management techniques in pediatric dentistry, there is an evident need for studies that address these outcomes, since dentists advance in using alternative methods for caries removal as part of their everyday practice.

Trial status

The trial is not yet recruiting patients. The process will start in September 2021 and will continue until September 2022.

Word count: 3705

Acknowledgements

The authors would like to show their gratitude to Assoc. Prof. Georgi Tomov, PhD for the fruitful discussion. Assistance with the Laser Center of the Faculty of Dental Medicine, Medical University of Plovdiv, Bulgaria was greatly appreciated. The authors are also thankful to Prof. Nonka Mateva, PhD for the statistical consultancy expertise in the planning of this clinical trial.

Author Contributions

We declare that all authors have made substantial contributions. MS and AB conceive the ideas. AB trained MS. MS will be the primary operator, outcomes assessor, and data collector. All authors will participate in the analysis and reporting of the results. Writing will be led by MS. The design and protocol for this study were developed by AB and MS. All authors contributed to refining the study protocol and approving the final manuscript.

Funding

This research received institutional funding from the Medical University – Plovdiv, Bulgaria.

Competing interests

None declared.

Patient consent for publication

(see Supplementary data file S1 `Patient consent form`)

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Consent form

For a patient's consent to publication of images and/or information about them in BMJ publications.

Name of patient: ______________________________

Patient`s parent/guardian: ______________________________

Material – text (information about your child`s oral health, level of dental anxiety and dynamics of heart rate): ______________________________

Provisional title of article in which Material will be included: Efficacy of Combined Er:YAG Laser Therapy and Behaviour Management Technique in Reducing Anxiety among Paediatric Dental Patients

____

CONSENT

I______________________________*[ENTER YOUR FULL NAME]* give my consent for the Material about my child to appear in a BMJ publication.

I confirm that I: *(please tick boxes to confirm)*

- ☐ ***have seen the text or other material about my child***
- ☐ ***have read the article to be submitted to BMJ***
- ☐ ***am legally entitled to give this consent.***

I understand the following:

(1) The Material will be published without my child`s name attached, however I understand that complete anonymity cannot be guaranteed. It is possible that somebody somewhere may recognise my child.

(2) The Material may show or include details of my child's medical condition or injury and any prognosis, treatment or surgery that I have/the patient has, had or may have in the future.

(3) The article may be published in a journal which is distributed worldwide. BMJ's publications go mainly to doctors and other healthcare professionals but are also seen by many others including academics, students and journalists.

(4) The article, including the Material, may be the subject of a press release, and may be linked to from social media and/or used in other promotional activities. Once published, the article will be placed on a BMJ website and may also be available on other websites.

(5) The text of the article will be edited for style, grammar and consistency before publication.

(6) I and my child will not receive any financial benefit from publication of the article.

Patient consent form 050419

(7) The article may also be used in full or in part in other publications and products published by BMJ and/or by other publishers. This includes publication in English and in translation, in print, in digital formats, and in any other formats that may be used by BMJ or other publishers now and in the future. The article may appear in local editions of journals or other publications, published in the UK and overseas.

(8) I can revoke my consent at any time before publication, but once the article has been committed to publication ("gone to press") it will not be possible to revoke the consent.

(9) This consent form will be retained securely and in confidence by BMJ in accordance with the law, for no longer than necessary. Personal data provided in this form will be used and retained in accordance with BMJ's Privacy Policy available at https://www.bmj.com/company/your-privacy/.

Signed: ______________________ *Print name:* ______________________

Address: ______________________ *Email address:* ______________________

______________________ *Telephone no:* ______________________

** signing on behalf of the patient who is under the age of 18*

______________________ *Date:* ______________________

Corresponding author

Signed: ______________________

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Date: ______________________

Patient consent form 050419

INFORMATION LEAFLET

DEPARTMENT OF PAEDIATRIC DENTISTRY
LASER CENTER
FACULTY OF DENTAL MEDICINE,
MEDICAL UNIVERSITY OF PLOVDIV, BULGARIA

EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS

DESCRIPTION: You and your child are invited to participate in a research study on the efficiency of Er:YAG laser therapy in combination with behavior management technique in reducing anxiety among pediatric dental patients.

PROCEDURES: With your permission, we would like to collect information about your children`s dental anxiety before, during and after dental treatment of a caries lesion. This study does not involve any experiments, just preventive procedures and dental treatment, collection, and study of the required information.

RISKS AND BENEFITS: There are no anticipated risks associated with this study. You will not receive any direct benefit from participation.

TIME INVOLVEMENT: Your child`s participation in this study will not require more time from you other than for the first visit including an explanation of the study, oral examination and a preventive procedure (sealant application). The second appointment at 7-day recall will include dental treatment.

PAYMENTS: You will not be paid to participate in this study. You will not pay for the treatment of your child in this study.

PARTICIPANT'S RIGHTS: If you have read this form and have decided your child to participate in this research, please understand your participation is voluntary and you have the right to withdraw your consent or discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

The results of this research study may be presented at scientific or professional meetings or published in scientific journals. However, your identity will not be disclosed**.**

Thank you for your time and attention!

Name of parent/guardian .....

Signature of parent /guardian .....

Name of patient .....

Telephone number .....

Name of the dentist .....

Signature of the dentist .....

For additional information regarding the trial, you can contact us at the given address, emails, or phone numbers.

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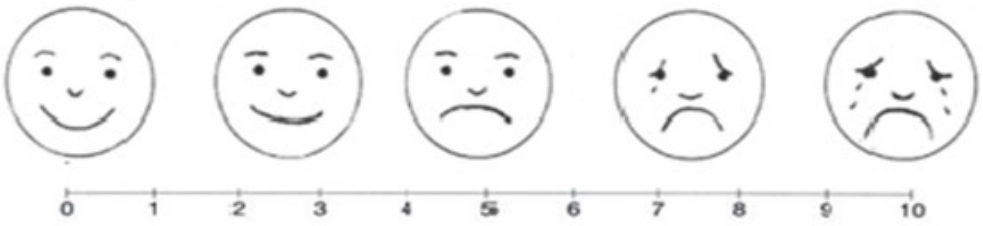

94x24mm (150 x 150 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	2,14
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	2
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3,4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3,4
Objectives	#7	Specific objectives or hypotheses	4

Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	4
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5,6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5,6
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	n/a
Interventions:	#11c	Strategies to improve adherence to intervention protocols,	n/a

adherance		and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests) Non-adherence interventions in the present study	
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial No permitted or prohibited during the trial concomitant care and interventions	n/a
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8,9
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Table 1)	9
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
Recruitment	#15	Strategies for achieving adequate participant enrolment to	9

		reach target sample size	
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a

		open-label trial	
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10,11
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10,11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11

Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	n/a
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			

Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11,12
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	11,12
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	12
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	12
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	12
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial	n/a

		participation	
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12,13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	12
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Suppl 1-3
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

BMJ Open

EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS: A STUDY PROTOCOL FOR A RANDOMIZED CLINICAL TRIAL

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-054523.R2
Article Type:	Protocol
Date Submitted by the Author:	21-Jun-2022
Complete List of Authors:	Belcheva, Ani; Medicinski universitet-Plovdiv, Department of Paediatric Dentistry Shindova, Maria; Medicinski universitet-Plovdiv, Department of Paediatric Dentistry
Primary Subject Heading:	Dentistry and oral medicine
Secondary Subject Heading:	Dentistry and oral medicine
Keywords:	Paediatric anaesthesia < ANAESTHETICS, Laser therapy < DERMATOLOGY, Child & adolescent psychiatry < PSYCHIATRY, Anxiety disorders < PSYCHIATRY

EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS: A STUDY PROTOCOL FOR A RANDOMIZED CLINICAL TRIAL

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Abstract

Introduction

When providing dental care to children with a high level of dental anxiety, the range of approaches are divided into two sections – use of behavior management techniques (BMTs) and application of alternative methods for caries removal. In an attempt to reduce dental anxiety, they can be mixed and matched in accordance with the dentists` choice. Owing to the promoted advantages Erbium-doped Yttrium Aluminium Garnet (Er:YAG) laser turns into an ideal alternative technique for hard

dental tissue therapy in anxious pediatric patients. The aim of the study is to assess the efficacy of a modified version of the BMT Latent inhibition in combination with Er:YAG laser for achieving a reduction of dental anxiety in pediatric dental patients.

Methods and analysis

This is a protocol for a randomized controlled clinical trial. The participants will be children aged 6-9 years, requiring conservative treatment of occlusal carious lesion on a second primary molar. Patients will be randomly assigned to the experimental or control group via a computer-generated sequence. In both groups, Latent inhibition will be used as an anxiety-management technique. In the experimental group caries treatment will be performed with Er:YAG laser, whereas in the control group with the conventional rotary instruments. Outcome measures will be dental anxiety felt before and after the treatment, reported by the patient on a modified version of Faces Scale by LeBaron and the dynamics of heart rate, registered during the treatment session, measured with a mobile pulse oximeter. Data will be analyzed by Independent sample t-test and paired t-test, $p<0.05$.

Ethics and dissemination

The study protocol has been approved by the Committee for Scientific Research Ethics, Medical University-Plovdiv, Bulgaria (Reference number P-2839, Protocol of approval No. 3/30.04.2015) and registered on a publicly accessible database. This research received institutional funding from the Medical University–Plovdiv, Bulgaria. The results will be presented through peer-reviewed publications and conference presentations.

Trial registration: ClinicalTrials.gov (Registration number: NCT04924452).

Keywords: Er:YAG laser, anxiety, management technique, pediatric dentistry

Article Summary

Strengths and limitations of this study

- The study focuses on the implementation of a known BMT in the alternative caries treatment method
- A key strength of this study is that all participants meeting eligibility criteria will receive active treatment.

- Both subjective and objective tools are used to assess dental anxiety in this study.
- A limitation of this study is that it is not a split-mouth design whose advantage is the reduction of the outcome variability estimation

1. Introduction

1.1. Background and rationale

When providing dental care to children with a high level of dental anxiety, most pediatric dentists find the conventional rotary treatment method inefficient and uncomfortable. According to the principles of behavioral dentistry, as part of pediatric postgraduate education, the so-called `4S` principle must be adapted and modified to the individual clinical situation to provide adequate dental care to anxious pediatric patients [1]. The range of approaches can be divided into two sections – behavior management techniques, on one hand, and alternative methods for caries removal, on the other hand. In an attempt to reduce dental anxiety, they can be mixed and matched in accordance with the dentists` choice.

As it has been found for more than 20 years that lasers are effective for caries excavation, Laser pediatric dentistry has been rapidly developed. It offers total innovation and changes the conventional restorative treatment in pedodontics [2]. Owing to the promoted advantages such as minimal intervention and prevention, safety due to the low penetration depth of the laser beam, selective removal of caries lesion, lack of thermal damage, no pain perception and use of local anesthesia, a significant decrease of patient discomfort and dental anxiety and increase of subjective acceptance and tolerance of laser therapy in children, Er:YAG laser turns into an ideal laser for hard dental tissue therapy in anxious pediatric patients [2,3,4].

Based on the concepts of Minimal Invasive Dentistry (MID), the use of BMTs during the treatment of anxious children to reduce their anxiety is required [5]. Several specific BMTs are not part of the regular curricula of dental students and have been used by pediatric dentists only [4,6,7]. Such a phycological technique is Latent inhibition also known as Gradual exposure [8,9]. It involves a series of several positive non-painful – check-ups and preventive procedures, before any invasive or painful dental manipulations. Step by step the child is exposed to potential anxiety-provoking procedures or instruments, resulting in an acquaintance with the dental setting and personnel, as well as being accustomed to dental treatment. Despite the specific indications, required preparation and higher time consumption, the use of this technique is very rewarding as the pediatric patient

eventually becomes comfortable with the dental procedure and creates a feeling of ability to cope within the child [6,7,10].

Over the recent years, dentists advance in using alternative methods for caries removal as part of their everyday practice. Therefore, the investigation of this synergetic effect of laser caries removal and the different BMTs is crucial for the present and future development of pediatric dentistry and will improve the quality of dental care.

1.2. Objectives

The aim of the study is to assess the efficacy of a modified version of the BMT Latent inhibition in combination with Er:YAG laser for achieving a reduction of dental anxiety in paediatric dental patients. The main objectives are to compare dental anxiety felt during the laser and conventional dental treatment. The outcomes will be dental anxiety assessment by self-reported anxiety scale during treatment in both groups as well as the measurement of heart rate dynamics during the procedures.

1.3. Trial design

The research is designed as a randomized parallel-group controlled clinical study. Table 1 presents the recruiting, allocation, interventions, monitoring, and analysis of the research in accordance with the Standard Protocol Items: Recommendations for Interventional Trials recommendations [11]. In accordance with the Latent inhibition technique patients will have two visits to the dental office – a preventive procedure, the first one, and treatment of caries lesion, the second one. Two groups will be compared. In the experimental group the enamel conditioning of the occlusal surfaces of the permanent molars before sealant application as well as the standardized caries treatment will be performed with Er:YAG laser, whereas in the control group the conventional rotary instruments - high-speed and low-speed dental handpieces, will be used for the caries treatment.

Table 1. Trial design. The table summarises the enrolment, allocation, interventions, and assessments in the trail

	STUDY PERIOD				
	Enrolment	**Allocation**	**Post-allocation**		
TIMEPOINT*	**$-t_1$**	**0**	**t_1**	**t_2**	**t_3**
ENROLMENT					
Eligibility screening	×				
Informed consent	×				
Allocation		×			
INTERVENTIONS					
Experimental group (BMT + Laser treatment of dental caries)				×	
Control group (BMT + Caries treatment with conventional rotary instruments)				×	
ASSESSMENTS					
Self-reported dental anxiety			×		×
Heart rate			◄	———	►

*Post-allocation time frame: t1 - before the start of the treatment; t_2 - during laser or conventional treatment; t_3 – end of the treatment, before leaving the dental chair.

2. Methods and analyses

2.1. Study setting

The study setting of this research includes the Department of Paediatric Dentistry and the Laser Centre of the Faculty of Dental medicine, Medical University – Plovdiv, Bulgaria.

2.2. Eligibility

2.2.1. Inclusion criteria

1. Participants in the study are children aged 6-9 years, compliant with the cognitive development of the child;
2. Children, requiring conservative treatment of occlusal carious lesions on a second primary molar, without spontaneous unprovoked pain, percussion or palpation pain or other symptoms, indicating pulp involvement or periodontal pathology. Lesions are classified as

a distinct cavity with visible dentin without prior restoration or sealants by the International Caries Detection and Assessment System (ICDAS) with code 05 [12,13,14]. Included are caries lesions only on vital teeth.

3. Children with one or more permanent molars giving indications for pit and fissure sealing;
4. Patients without previous experience with laser treatment of carious lesions;
5. Children who are not considered medically compromised or medically complex patients;
6. Verbal assent from the child willing to comply with all study procedures and protocol;
7. Obtained written informed consent by the patient`s parent/guardian for participation in the study (see supplementary data file S1 `Patient consent form` and S2 `Information leaflet`).

2.2.2. Exclusion criteria

1. Patients who were undergoing therapy with neurological, sedative, analgesic, and/or anti-inflammatory drugs 7 days prior to treatment that might affect heart rate;
2. Children, who were first-time dental patients;
3. Children with systemic diseases or physiological development delays;
4. Children with mental or cognitive problems;
5. Active infectious diseases such as influenza, scarlet fever, etc.
6. Excluded are molars which are affected by disturbances in the development of dental structures (hypoplasia, hypomineralization, fluorosis)

2.2.3. Interventions

Patients will be divided into 2 groups (41 per group) – experimental and control groups. All treatments will be carried out by the same operator (MS), without anesthesia. A baseline dental self-reported anxiety will be recorded using a Faces anxiety scale as well as the dynamics of heart rate, measured with a mobile pulse oximeter.

Er:YAG laser therapy protocol (experimental group):

Er:YAG laser (LiteTouch, Light Instruments LTD), emission wavelength 2940 nm will be used for enamel conditioning of the occlusal surfaces of the permanent molars before sealant application as well as the standardized caries treatment. Chosen protocol parameters are modified based on previously conducted studies [2,3,4,15,16]:

- preventive procedure – sealant application:

- a low-speed rubber cup and pumice paste (CleanPolish, Kerr) will be used for 30 seconds for cleaning and polishing of the occlusal surface of the chosen permanent molar;
- tooth surface will be washed for debris and organic residue removal and dried with air spray;
- isolation with rubber dam;
- laser conditioning of the occlusal enamel surface. The parameter settings used will be: tip-to-tissue distance 1.5mm from the tooth surface; tip diameter 600 μm; laser energy 70 mJ; pulse frequency 10 Hz; water spray level 8; average power 0.7 W; energy density 67 J/cm^2;
- tooth surface will be etched with 35% phosphoric acid gel (Etching gel, DMP Ltd) for 30 seconds and rinsed for the same time;
- tooth surface will be dried with air spray for 15s;
- fissure sealant application (Pit&Fisssure Sealant, DMP Ltd);
- light cured for 20 seconds.

caries removal – parameters: enamel removal – energy 100-200mJ; density 9.84-13.03 J/cm^2, pulse frequency 20Hz; tip diameter 800 μm; water spray level 8; tip-to-tissue distance 0.5÷1 mm from the tooth surface; dentin removal - energy 100mJ; density 9.84 J/cm^2, pulse frequency 20Hz; tip diameter 800 μm; water spray level 8; tip-to-tissue distance 0.5÷1 mm form the tooth surface. Restoration with compomer. Time for caries removal procedure – max 8 minutes [17,18,19,20].

Conventional therapy protocol (control group):

- preventive procedure – sealant application

- a low-speed rubber cup and pumice paste (CleanPolish, Kerr) will be used for 30 seconds for cleaning and polishing of the occlusal surface of the chosen permanent molar;
- tooth surface will be washed for debris and organic residue removal and dried with air spray;
- isolation with rubber dam;
- tooth surface will be etched with 35% phosphoric acid gel (Etching gel, DMP Ltd) for 30 seconds and rinsed for the same time;
- tooth surface will be dried with air spray for 15s;
- fissure sealant application (Pit&Fisssure Sealant, DMP Ltd);
- light cured for 20 seconds.

- caries removal – conventional rotary instruments will be used - high-speed and low-speed dental handpieces. For the bur preparation 1.2 mm diameter diamond round bur Drendel &

Zweiling No. 801.314. and Komet Steel round bur 016, Komet Dental Gebr were used. A new bur was used for each preparation. Restoration with compomer. Time for caries removal procedure – max 4 minutes.

2.2.4. Clinical protocol

First visit:

1. Parents/guardians are informed about the protocol of the study and the laser technique. They sign the informed consent form (see Supplementary data files S1 and S2). Verbal assent from the child is obtained.
2. Oral examination and sealant application are performed according to the assigned intervention.
3. Patient`s self-report of dental anxiety before leaving the dental chair.

Second visit:

1. Patients will be asked to report their dental anxiety, pointing to the face or choose the number which most closely depicted its state of anxiety using a modified version of the self-report Faces Scale by LeBaron et al. [21] (see Supplementary data file S3)
2. Pulse-oximeter is connected to the patient`s index finger. The start of heart rate monitoring and recording will be 5 minutes prior to treatment. Time frame: at least 5 minutes after the dental treatment, before leaving the dental chair.
3. Caries treatment is performed according to the assigned intervention.
4. Patient`s self-report of dental anxiety before leaving the dental chair.

2.3. Outcomes

2.3.1. Primary outcome measures

The primary outcome will be the dental anxiety before and after the treatment session, reported by the patient on a modified version of the self-report Faces Scale by LeBaron et al.. The scale comprises a row of five faces ranging from `relaxed` to `very worried` in combination with a visual analog scale of 0 – 10. Each child was asked to point to the face or choose the number which most closely depicted its state of anxiety.

2.3.2. Secondary outcome measures

The secondary outcome will be the dynamics of heart rate, registered during the treatment session measured with a mobile pulse oximeter (CMS50F, CONTEC), placed on the index finger of the left hand [22]. Throughout the whole procedure of each dental visit, data were recorded and

analyzed by a specially developed digital processing and graphic visualization software SPO2 Review V1.2 rel.

2.3.3. Participant`s timeline

Each eligible patient undergoes two visits. The first appointment includes screening, consenting and assenting, recording of dental anxiety, sealant application according to the assigned interventions for each group. The second appointment at the one-week recall includes a recording of dental anxiety and treatment of a carious lesion according to the assigned interventions for each group. The manipulations will be performed by one operator.

2.3.4. Sample size calculation

The sample size calculation is performed based on data from a pilot study with 20 subjects. To estimate sample size for the primary outcome—self-reported anxiety felt, according to the Faces Scale by LeBaron —a t-test for paired groups has been used (G* Power software V.3.1,6 since we have two groups). The effect size was determined using the formula

$$ES = \frac{Control - Treated}{SDpooled} = \frac{2.33 - 0.33}{3.25} = 0.62$$

where SD is the pooled SD, an average of the SD of the experimental and control groups. The sample size is calculated to assure a test power greater than 95% and a significant level of $\alpha = 0.05$. We estimated a sample size of 41 patients per group to detect significant differences. Thus, the final sample size for this study will be 82 patients.

2.4. Recruitment

The patients at the Department of Paediatric Dentistry of the Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria, who meet the inclusion criteria, will be screened for eligibility. Once identified, patients will be informed about this research project and will receive information about the possibility of potential study participation. Patient recruitment starts obtaining the full quota of participants within a one-year time frame. It begins in September 2021 with an estimated enrollment capacity of 5 patients per month.

2.5. Participating centers

The patients are randomly selected from the visitors in the Department of Paediatric Dentistry of the Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria, and treated in the Laser Centre of the same university.

2.6. Assignment of the intervention

2.6.1. Sequence generation

The patients will be randomly allocated to either the control group or the experimental group (41 patients in each group) according to the enrolment number in the trial. The randomization will be created using a computerized random generator.

2.6.2. Allocation concealment mechanism and implementation

A randomization list will be created by a random generator before the start of the treatment and kept in a locked drawer. Assignments will be kept in separate, closed opaque, sequentially numbered envelopes, enabling the sequence to be concealed until the intervention is assigned.

2.6.3. Blinding

The randomisation will be independent, that is, the patients and parents/guardians will remain blinded to group status. The operator will get acquainted with the procedure to be performed prior to the first session. The operator is selected to be the only one performing the manipulation to prevent bias. The statistician will be blinded to treatment assignment as data will be masked before the analysis without giving the statistician the key.

2.6.4. Data collection, confidentiality, storage, and monitoring of the study documents

Collection, coding, storage, and evaluation of personal data within the project will be carried out in accordance with The General Data Protection Regulation *(*EU*)* 2016/679 (*GDPR*). A prerequisite for data collection will be the voluntary written informed consent of the patient`s parent or guardian. Confidentiality will be guaranteed by a coded ID number, access will be granted exclusively to the study investigators. The information from the paper forms will be exported to a database file and stored on a password-protected computer. Only the investigators and statistician will have access to the final data set. All data collected will be stored in sealed containers in areas of the Department of Paediatric Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria with limited access.

3. Statistical methods

The obtained data will be recorded, tabulated, processed, and analyzed using SPSS (Statistical Package for Social Science software) version 21.0 (IBM, USA). In all tests, the significance level of 5% probability or the corresponding *P*-value will be adopted. Descriptive statistics will be calculated. Discrete variables will be summarised by frequencies or proportions. Continuous variables will be presented as means and standard deviations. We will compare anxiety mean scores according to the Faces Scale by LeBaron as well as heart rate mean score. Comparisons among groups will be performed by using the Independent sample t-test and paired t-test.

4. Patient and public involvement

The development of the research question and outcome measures will be based on the review of available evidence in this research area. Patients will not be involved in the development of the study protocol. However, their questions and concerns will be addressed during patient recruitment and study implementation. During the conduction of the study, patients will not be informed about the results of the ongoing trial since there is no planned interim analysis. The results will be disseminated to the study participants through email and routine follow-up dental check-ups.

5. Ethics and dissemination

The clinical study will be conducted in accordance with the conditions and principles of the Declaration of Helsinki, the existing EU Clinical Trial Directive (EC) No. 2001/20/EC, the recommendations of the Ethical Committee at the Medical University of Plovdiv, Bulgaria and the international ethical and scientific quality standard for designing, recording and reporting trials that involve the participation of human subjects - Good Clinical Practices (GCP).

5.1. Research ethics approval

The study was approved by the Committee for Scientific Research Ethics, Medical University - Plovdiv, Bulgaria (Reference number P-2839, Protocol of approval No.3/30.04.2015) and registered on a publicly accessible database ClinicalTrials.gov (Registration number: NCT04924452). Ethical approval for the study protocol and the written informed consent for all subjects` parents/guardians was granted by the Ethics Committee of the Medical University, Plovdiv, Bulgaria.

5.2. Consent

The operators will obtain written consent from patients` parents/guardians willing to participate in the trial. Additional information will be provided for all parents for the study. Completed informed consent will be collected at the Department of Pediatric Dentistry, Medical University - Plovdiv by the study investigators. A copy of the signed consent form will be handed over to the participating child`s parent/guardian. After providing age-appropriate information about the study, verbal assent will be obtained as an affirmative agreement for participation from children

5.3. Confidentiality

The information of the participants collected during the study will be kept strictly confidential and will not be disclosed to third parties. Confidentiality will be guaranteed by a coded ID number, access will be granted exclusively to the study investigators.

5.4. Conflict of interests

The investigators have no conflicts of interest to declare. They agree with the protocol and the informed consent of the study and there is no financial interest to report.

5.5. Access to data

All data collected will be stored in sealed containers in areas of the Department of Paediatric Dentistry, Faculty of Dental Medicine, Medical University – Plovdiv, Bulgaria with limited access. The information from the paper forms will be exported to a database file and stored on a password-protected computer. Only the investigators and statistician will have access to the final data set.

5.6. Dissemination policy

The results of the trial will be presented through peer-reviewed publications and conference presentations. In addition, our results will be disseminated to clinicians, as well as key stakeholders, including scientific directors of postgraduate programs "Master of Science in Lasers in Dentistry", academic courses in Pedodontics and Preventive dentistry. The principle investigator (MS) and the scientific expert (AB) will write the first draft of the manuscript without the use of professional writers.

Trial status

The trial is not yet recruiting patients. The process will start in September 2021 and will continue until September 2022.

Word count: 3705

Acknowledgements

The authors would like to show their gratitude to Assoc. Prof. Georgi Tomov, PhD for the fruitful discussion. Assistance with the Laser Center of the Faculty of Dental Medicine, Medical University of Plovdiv, Bulgaria was greatly appreciated. The authors are also thankful to Prof. Nonka Mateva, PhD for the statistical consultancy expertise in the planning of this clinical trial.

Author Contributions

We declare that all authors have made substantial contributions. MS and AB conceive the ideas. AB trained MS. MS will be the primary operator, outcomes assessor, and data collector. All authors will participate in the analysis and reporting of the results. Writing will be led by MS. The design and protocol for this study were developed by AB and MS. All authors contributed to refining the study protocol and approving the final manuscript.

Funding

This research received institutional funding from the Medical University – Plovdiv, Bulgaria.

Competing interests

None declared.

Patient consent for publication

(see Supplementary data file S1 `Patient consent form`)

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Consent form

For a patient's consent to publication of images and/or information about them in BMJ publications.

Name of patient:	______________________
Patient`s parent/guardian:	______________________
Material – text (information about your child`s oral health, level of dental anxiety and dynamics of heart rate):	______________________
Provisional title of article in which Material will be included:	Efficacy of Combined Er:YAG Laser Therapy and Behaviour Management Technique in Reducing Anxiety among Paediatric Dental Patients ______________________

CONSENT

I______________________________________*[ENTER YOUR FULL NAME]* give my consent for the Material about my child to appear in a BMJ publication.

I confirm that I: *(please tick boxes to confirm)*

- ☐ ***have seen the text or other material about my child***
- ☐ ***have read the article to be submitted to BMJ***
- ☐ ***am legally entitled to give this consent.***

I understand the following:

(1) The Material will be published without my child`s name attached, however I understand that complete anonymity cannot be guaranteed. It is possible that somebody somewhere may recognise my child.

(2) The Material may show or include details of my child's medical condition or injury and any prognosis, treatment or surgery that I have/the patient has, had or may have in the future.

(3) The article may be published in a journal which is distributed worldwide. BMJ's publications go mainly to doctors and other healthcare professionals but are also seen by many others including academics, students and journalists.

(4) The article, including the Material, may be the subject of a press release, and may be linked to from social media and/or used in other promotional activities. Once published, the article will be placed on a BMJ website and may also be available on other websites.

(5) The text of the article will be edited for style, grammar and consistency before publication.

(6) I and my child will not receive any financial benefit from publication of the article.

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(7) The article may also be used in full or in part in other publications and products published by BMJ and/or by other publishers. This includes publication in English and in translation, in print, in digital formats, and in any other formats that may be used by BMJ or other publishers now and in the future. The article may appear in local editions of journals or other publications, published in the UK and overseas.

(8) I can revoke my consent at any time before publication, but once the article has been committed to publication ("gone to press") it will not be possible to revoke the consent.

(9) This consent form will be retained securely and in confidence by BMJ in accordance with the law, for no longer than necessary. Personal data provided in this form will be used and retained in accordance with BMJ's Privacy Policy available at https://www.bmj.com/company/your-privacy/.

Signed: ______________________ *Print name:* ______________________

Address: ______________________ *Email address:* ______________________

______________________ *Telephone no:* ______________________

** signing on behalf of the patient who is under the age of 18*

______________________ *Date:* ______________________

Corresponding author

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Patient consent form 050419

INFORMATION LEAFLET

DEPARTMENT OF PAEDIATRIC DENTISTRY
LASER CENTER
FACULTY OF DENTAL MEDICINE,
MEDICAL UNIVERSITY OF PLOVDIV, BULGARIA

EFFICIENCY OF ER:YAG LASER THERAPY IN COMBINATION WITH BEHAVIOUR MANAGEMENT TECHNIQUE IN REDUCING ANXIETY AMONG PAEDIATRIC DENTAL PATIENTS

DESCRIPTION: You and your child are invited to participate in a research study on the efficiency of Er:YAG laser therapy in combination with behavior management technique in reducing anxiety among pediatric dental patients.

PROCEDURES: With your permission, we would like to collect information about your children`s dental anxiety before, during and after dental treatment of a caries lesion. This study does not involve any experiments, just preventive procedures and dental treatment, collection, and study of the required information.

RISKS AND BENEFITS: There are no anticipated risks associated with this study. You will not receive any direct benefit from participation.

TIME INVOLVEMENT: Your child`s participation in this study will not require more time from you other than for the first visit including an explanation of the study, oral examination and a preventive procedure (sealant application). The second appointment at 7-day recall will include dental treatment.

PAYMENTS: You will not be paid to participate in this study. You will not pay for the treatment of your child in this study.

PARTICIPANT'S RIGHTS: If you have read this form and have decided your child to participate in this research, please understand your participation is voluntary and you have the right to withdraw your consent or discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

The results of this research study may be presented at scientific or professional meetings or published in scientific journals. However, your identity will not be disclosed**.**

Thank you for your time and attention!

Name of parent/guardian .....

Signature of parent /guardian .....

Name of patient .....

Telephone number .....

Name of the dentist .....

Signature of the dentist .....

For additional information regarding the trial, you can contact us at the given address, emails, or phone numbers.

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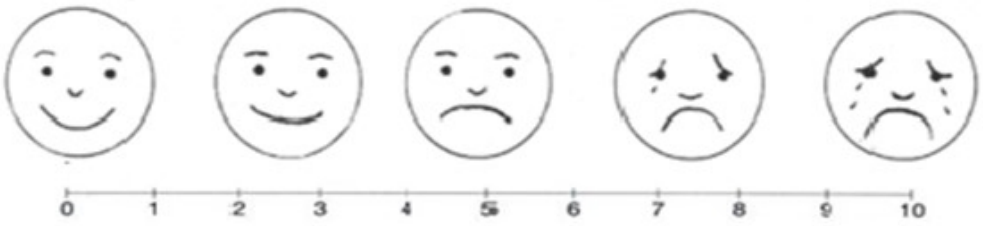

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Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	2,14
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	2
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3,4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3,4
Objectives	#7	Specific objectives or hypotheses	4

Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	4
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	5,6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5,6
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	n/a
Interventions:	#11c	Strategies to improve adherence to intervention protocols,	n/a

adherance		and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests) Non-adherence interventions in the present study	
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial No permitted or prohibited during the trial concomitant care and interventions	n/a
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8,9
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Table 1)	9
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
Recruitment	#15	Strategies for achieving adequate participant enrolment to	9

		reach target sample size	
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a

		open-label trial	
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10,11
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10,11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11

Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	n/a
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			

Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11,12
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	11,12
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	12
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	12
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	12
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial	n/a

		participation	
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12,13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	12
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Suppl 1-3
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a