Effects of Photobiomodulation on Postoperative Pain After Primary Endodontic Therapy in Molars With Symptomatic Apical Periodontitis

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Protocol Title: Effects of photobiomodulation on postoperative pain after primary endodontic therapy in mandibular molars with symptomatic apical periodontitis

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Population: Sample size = 52 adult patients ages 18 and older divided into two groups (intervention group and control group)

Number of Sites: 1 site; UT School of Dentistry Graduate Endodontic Clinic

Study Duration: One year - Two academic semesters

Subject Duration: One dental visit - approximately 2 hours

General Information

Teeth diagnosed with SAP are more prone to present postoperative pain even after root canal therapy (RCT) is completed. Photobiomodulation (PBM) has been used for decades in medicine and dentistry showing promise results in the healing capabilities, however, an accepted protocol has still not been created for its regular use in endodontics. PBM utilizes the body's own hardware by working specifically on the mitochondria in cells to improve patient healing and reduce post-treatment pain. The mitochondrial events taking place during PBM are thought to be: increased ATP production, release of nitric oxide, and release of reactive oxygen species. All of these events lead to an increase in cellular mediators involved in inflammation and pain control and thus PBM can greatly improve the outcomes of our endodontic treatment on these teeth.

The aim of this clinical study is to investigate the use of PBM after primary root canal therapy in mandibular molars diagnosed with symptomatic apical periodontitis (SAP) to reduce postoperative pain.

Fifty-twodult patients will be invited to participate in this study. They will be divided in 2 groups: Control group where patients will receive conventional RCT (n=26) and PBM group where patients will receive conventional RCT plus PBM immediately post-operatively (n=26). Pre-operative and postoperative pain will be accessed by using a visual analogue pain scale. Data will be analyzed using continuous ordinal regression and distribution-free methods (Wilcoxon, Mann-Whitney tests)

Background Information

One of the main goals of endodontic (root canal) therapy is to eliminate pain. It has been well described in the literature that certain teeth tend to hurt more after root canal therapy. Preoperative pain intensity, pain interfering with daily activities, pain made worse with stress,

and diagnosis of symptomatic apical periodontitis were all listed as independent predictors of severe pain intensity following root canal therapy (Law et al, 2015). Another study looked at similar predictors of postoperative pain and found mandibular molars to have significantly more postoperative pain than maxillary molars (Sadaf, 2014).

Our everyday options for post-treatment pain is mostly limited to various prescription medications. This should be considered a major limitation especially in today's world where we are fighting an active opioid crisis.

According to the CDC, from 1999-2019 nearly 841,000 people died from an overdose involving prescription and illicit opioids. Nearly 247,000 Americans lost their lives to overdoses involving prescription opioids in the same two-decade time period. The good news is that the trend is now declining and doctors are prescribing opioids with much more caution. From 2006-2017 there was a 19% reduction in annual prescribing of opioids but the amount of opioids in morphine milligram equivalents (MME) prescribed per person is still around 3x what it was in 1999.

Today, we know through an overwhelming amount of evidence that NSAIDS, Acetaminophen, and long-acting local anesthetics may result in greater analgesia for our patients than opioids. Acetaminophen and NSAIDS are great in dealing with pain, however their effectiveness is rather limited. Both Acetaminophen and NSAIDS are subject to a ceiling dosage with regard to effective analgesia. This means that past a certain dosage, the patient cannot achieve any greater pain relief than what was provided before they reached that ceiling dose. The point is – there are dozens of unique situations where practitioners need to have more tools available in dealing with pain when the standard protocol is ineffective.

One such way of dealing with this pain is using Photobiomodulation (PBM), also known as low-level light therapy (LLLT), to deal with post-treatment pain. Photobiomodulation's effects on accelerating the healing process were introduced in the 1960s but its use in dentistry is still not all that commonplace. The generally accepted mechanism of action is that absorbed light from the laser on the target tissue creates reactive oxygen species which leads to gene transcription and cellular healing. Mitochondria are very receptive to this process and the near-infrared light is absorbed and the energy is converted into ATP for cellular functions. Cytochrome C is key to this process as it is a chromophore and accepts the light to move these processes forward—at least that is the current level of thinking on the subject. There have been many studies showing the effects of PBM on healing in various medical specialties including dentistry but an accepted protocol has not yet been standardized. The Grotthus-Draper law or law of photochemical activation states that only light which is absorbed by a system can bring about a photochemical change. The correct wavelength for the target cells chromophores to induce the desired effect of PBM is 633 – 830 nm according to Kim and Calderhead. In this study, we will be using 660 nm to achieve our desired and expected results with PBM.

Objective:
The aim of this study is to evaluate the effects of photobiomodulation (PBM) on postoperative pain after endodontic treatment in mandibular molar teeth diagnosed with symptomatic apical periodontitis.

Study Design:

This randomized clinical trial is designed to evaluate the effects of photobiomodulation (PBM) on patients with symptomatic apical periodontitis (SAP) receiving root canal therapy.
Fifty-two patients (n=52) diagnosed with SAP will be selected and invited to participate in the study.

The inclusion criteria:

- Patients over 18 years old
- Posterior mandibular molars
- No previous root canal therapy on the tooth in question
- Able to complete the endodontic treatment in one visit

The exclusion criteria:

- Maxillary teeth, mandibular anteriors and premolars
- Infection (swelling, sinus tract) on the tooth in question
- Periodontal disease on the tooth in question
- Dental trauma
- Crown/ root fractures
- Bone marrow transplant or other organ transplant patients who are on chemical immunosuppressants
- Uncontrolled HIV disease
- Patients at risk for delayed or compromised wound healing

Note: Patients who are HIV positive and taking ART with undetectable viral load and a CD4 cell count above 400 are not considered immunocompromised

The group distribution treatment will be done by the investigators by computer-generated randomization (Research Randomizer). Patients will be randomly divided into two groups:

(A) experimental group - patients will receive root canal and PBM treatment.
(B) control group - patients will receive root canal and PBM sham treatment.

Patients will be informed of the details of study procedures. They will have the opportunity to ask questions. The consent form will be presented and discussed with patients and should be signed before the procedure. A single calibrated operator will perform all of the treatments (root canal therapy, PBM, and PBM sham treatments).

<u>Pre-treatment pain assessment</u>

The operator will ask the patient to rate pain level before starting the endodontic treatment.
A Visual Analogue Scale (VAS) will be provided to the patient and is used as a pictorial tool to help patients quantify their pain level: 1-3 = mild pain; 4-6 = moderate pain; 7-10 = severe pain. (Figure 1)

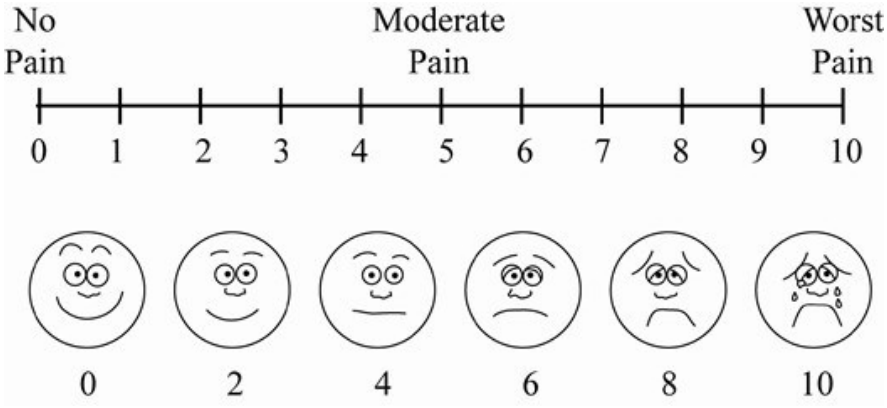


Figure 1. Illustration of the Visual Analogue Scale (VAS).

Endodontic Treatment

Patients will be anesthetized using 1.76 ml of 0.5% marcaine with 1:200,000 epinephrine via inferior alveolar nerve block, 1.76 mL 2% lidocaine with 1:100,000 epinephrine via inferior alveolar nerve block, and 1.76 mL of 4% Articaine with 1:200,000 epinephrine via infiltration.

Conventional endodontic treatment will be performed as follows: radiographs, dental dam isolation, straight-line access, cavity preparation, working length determined using an electronic apex locator, and a #10 K file. Canals will be prepared using Vortex Blue rotary instrumentation with 0.04 taper according to manufacturer's instructions and the #10 K file used for patency at the beginning of the procedure.
Irrigation will be performed with 10 mL of 6% sodium hypochlorite with in-and-out pecking motions, and a final rinse using 5 mL of 17% EDTA for 1 minute followed by 4 mL of 6% NaOCl for 1 minute. Irrigant activation will be completed prior to final rinse using an XP Endo Finisher (FKG Dentaire. La-Chaux-de-Fonds, Switzerland) file for 60 seconds using slight in-and-out movements.
After root canal preparation, the root canals will be dried with paper points and filled using matched single cones and CeraSeal(MetaBiomed, America) – a calcium silicate-based sealer. Final radiograph will confirm final canals obturation.
The pulp chamber will be etched with 35% phosphoric acid for 15 seconds, rinsed and gently dried, bonding agent (OptiBond® Solo Plus™, Kerr Corporation, Brea, CA, USA) will be applied, gently air-dried and light-cured for 20 seconds. Permaflo purple (Ultradent, America) composite resin will be used to seal the canals and light-cure for 20 seconds. Tooth will be restored with a glass ionomer (Fuji IX, GC America, USA) to seal the access cavity using a bulk fill technique.

Photobiomodulation Treatment

Immediately after the endodontic treatment, PBM therapy or sham will be performed using a 660 nm diode laser (SiroLaser Advance Plus, Dentsply Sirona Inc, Charlotte, NC, USA), with an 8mm tip diameter. The laser tip will be placed on the following external surfaces in a contact mode: mesiobuccal, distobuccal, mesiolingual and distolingual (Figure 1). The power output of the laser will be 50mW and will be verified by Power Meter (PM600 Power/Energy meter,

Molectron Detector Inc, Portland, OR, USA). Each site will be irradiated for 25 s with an energy density of 10 J/cm^2 .
For the PBM sham similar procedure will be performed without activating the laser.

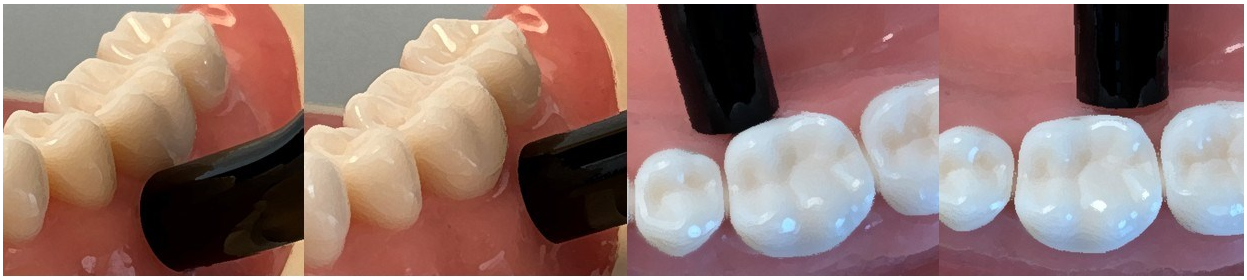


Figure 2. Illustration of laser tip positioning

Patient Dismissal

At the completion of treatment, patients will be given both verbal and written post-op instructions along with a pain diary form to be completed at home (Figure 3). No pain measurement will be taken after the procedure as the patient is anesthetized. Assuming no contraindications patients will be instructed to take 400 mg Ibuprofen with 500mg extra strength Tylenol as needed for pain. If another pain medication is to be administered the reason will be well documented and the patients VAS scores may be excluded as this could be a potential confounding variable. All dosages of pain medication will be recorded.

If patients are experiencing severe pain it will be recommended to take 400 mg Ibuprofen with 500 mg extra strength Tylenol. If a subject cannot be reached at a specific time point they will simply be asked to recall to the best of their ability their pain score at that time level when they are reached. If a patient continually cannot recall their VAS score or stops responding their data will be excluded.

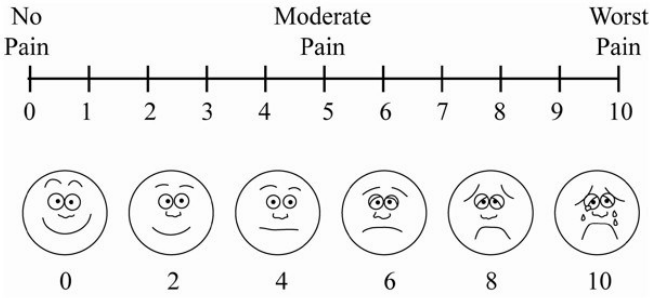
Outcome Measures

Patient pain as assessed by score on pain scale (see visual analog scale below), end of follow up period is 6 months. Patients will be asked for their pain scale responses at 6 hr, 12hr, 24hr, and 72 hrs after treatment is completed.

Primary outcome measure: Patient pain as assessed by score on pain visual analogue scale at 72 hours

Secondary outcome measures: Patient pain as assessed by score on pain visual analogue scale at 6hrs, 12hrs, 24hrs

PAIN DIARY FORM



Timeline	Date & Hour	Pain Level - VAS	Pain medication & dosage
Prior to RCT			
6 hrs. after RCT			
12 hrs. after RCT			
24 hrs. after RCT			
72 hrs. after RCT			

Figure 3. Pain Diary Form to be completed by the patient at home.

Post-treatment pain assessment

Patients will be contacted via phone at 6, 12, 24, and 72-hour intervals. The pain level will be recorded by a blinded investigator. In addition, patients will be asked to self-report any pain medication intake.

Risks and benefits

Risks are minimal as photobiomodulation has not been shown to have any negative effects on the teeth and it potentially can reduce pain and improve healing after root canal therapy.

Photobiomodulation will be performed using a 660nm red laser, which may have eye hazard risks. All safety protocols will be followed including laser safety wavelength-specific goggles by everyone in the operatory including the patient. The operator is laser certified and has been trained in laser safety protocols.

Study Population

Patients, 18 years and older, with symptomatic apical periodontitis (SAP) receiving endodontic treatment in one visit from the UT Health Science Center, Graduate Endodontic Dental Clinic.

Data and Safety Monitoring

No adverse effects are expected. All patients will be de-identified. During the study, data will be securely stored on encrypted computers or in a locked file cabinet with access limited to study personnel. Subject confidentiality and anonymity will be maintained throughout the study.

Statistics

Statistics to analyze collected data will include a 95% confidence interval of mean outcome measures that will be calculated for each treatment group. The significant level for the statistical test will be $p < 0.05$.

Publication Plan

Results will be submitted to a professional journal for consideration for publication.

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