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Original Research

A Comparative Study of the Effectiveness of Immediate Versus Delayed Photobiomodulation Therapy in Reducing the Severity of Postoperative Inflammatory Complications

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Abstract

Objective: The aim of this study was to compare the immediate versus the delayed application of photobiomodulation (PBM) therapy following odontectomy of horizontally impacted mandibular third molars, and assess which application method is more effective at reducing postoperative complications. ***Background data:*** Surgical removal of horizontally impacted mandibular third molars is a common surgical procedure, usually associated with postoperative complications such as pain, swelling, and trismus. Several attempts have been made to minimize these complications. One such method is the use of PBM therapy. ***Methods:*** Eighty patients with horizontally impacted mandibular third molars with no inferior alveolar canal approximation were recruited for this study. They were divided into two groups. The immediate group received PBM therapy immediately after surgery and on the 3rd day postoperatively. Subjects in the delayed group received PBM therapy on the 2nd and 4th days postoperatively. All subjects received 2 min of treatment using a 4 W laser beam, during which 171 J were delivered via a 2.8 cm^2 spot size. ***Results:*** Clinical and statistical results showed a significant reduction in pain, trismus, and swelling in the immediate PBM therapy group compared with the delayed PBM therapy group. ***Conclusions:*** Immediate PBM therapy is more effective than delayed PBM therapy in minimizing the complications associated with mandibular third molar removal surgery.

Introduction

Impacted teeth are defined as those teeth that are prevented from eruption into their normal position because of lack of space or other impediments.[1,2] They are considered a pathologic condition that requires management in the form of surgical removal. The surgical procedure, however, involves the manipulation of both soft and bony tissues and is, therefore, associated with postoperative complications such as pain, trismus, and swelling.[3] These complications are a manifestation of the inflammatory processes that ensue following surgical trauma.[4,5]

Throughout the literature and over the years, authors have recognized the value of comprehensive treatment planning in minimizing postoperative complications, because it allows surgeons to modify their surgical technique accordingly. Preoperative assessment should include a detailed history of the case, a thorough clinical examination, and adequate imaging examination in order to accurately classify the impacted tooth and localize it in relation to neighboring vital structures.[6–8] Imaging examinations usually consist of a panoramic radiograph that may be supplemented with intraoral periapical radiographs. However, these images are limited by their two dimensional (2D) nature. More recently, cone beam computed tomography (CBCT) has become the preferred imaging modality for assessment of impacted teeth. It offers many advantages such as submillimeter spatial resolution and relatively low radiation doses when compared with multidetector CT.

Prescribed medications such as corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs) are an integral part of a surgeon's armamentarium to relieve pain, trismus, and swelling following third molar surgery. However, these medications carry side effects and may be contraindicated for some patients. Therefore, there is a pressing need to find an alternative with no side effects. Photobiomodulation

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(PBM) therapy, previously known as low-level laser therapy, is believed to be one potential alternative. First used in 1966, it was not until 1977 that reports of the use of PBM therapy in the practice of oral and maxillofacial surgery appeared.[9,10] PBM therapy has acclaimed analgesic and anti-inflammatory effects that potentially can lead to a speedier recovery of patients following surgery. These effects of PBM therapy have been extensively investigated in patients undergoing surgical removal of impacted third molars; however, the results have been variable and controversial. We hypothesize that this maybe related to the timing of PBM therapy. Therefore, the aim of this study was to compare the effects of immediate versus delayed application of PBM therapy on the severity of pain, trismus, and swelling following surgical removal of horizontally impacted mandibular teeth.

Materials and Methods

After approval by the local ethical committee, 80 patients referred to the oral and maxillofacial surgery outpatient clinic were recruited into this prospective clinical study over a 1-year time period. Inclusion criteria included adult patients with at least one horizontally (as per Winter's classification) impacted mandibular molar in position B (according to Pell and Greg classification) with no mandibular canal approximation as determined by imaging. The authors chose this classification of impaction specifically because it involves significant manipulation of soft and bone tissues. Patients with systemic diseases, those taking corticosteroids or NSAIDs, and smokers were excluded from the study. A comprehensive history and a thorough clinical examination were performed. Basic demographic data such as age and gender were collected.

CBCT imaging was performed with the i-CAT CBCT unit (Imaging Sciences International, Hatfield, PA) using a 15-cm field-of-view (FOV) with the following exposure parameters: 120 kVp, 15 mA, and 0.3 mm voxel size. The patient's occlusal plane was parallel to the floor during the scan. The reformatted images were viewed using Vision software on a 48-cm Dell Ultrasharp 1907 flat panel LCD screen (Dell Inc. Round Rock, TX) with a maximum resolution of 1280×1024 pixels in a dimly lit room. Two certified specialists in oral and maxillofacial radiology reviewed the images after a calibration exercise that involved 10 archived cases. The aim of the calibration exercise was to standardize the classification of impacted third molars according to Winter's and Pell and Gregg classifications. The observers were blinded to any clinical data, but were allowed to view, enhance, and manipulate the entire image set. Disagreement was resolved by discussion and consensus.

The surgical procedure was standardized among the four performing oral and maxillofacial surgeons; the details of which were as follows. With the patient under local anesthesia using 2–3 carpules of lidocaine 2% with 1:100,000 epinephrine and sterilization of the surgical area, a triangular mucoperiosteal flap was elevated. Next, bone was removed based on imaging findings to free the tooth from any obstruction and provide a point of application for an elevator. Then the tooth was sectioned and elevated followed by wound irrigation with sterile 0.9% saline. Wound closure was achieved using 3-0 interrupted black silk sutures. The medication protocol included prophylactic antibiotics in the form of amoxicillin and clavulanate potassium 1 g. Paracetamol 500 mg was the analgesic of choice, given as needed with a maximum daily dose of 4000 mg. Chlorhexidine 0.2% mouthwash was prescribed starting from the 2nd day postoperatively and for 5 consecutive days.

All subjects were given daily appointments for the 1st postoperative week. Subjects were randomly divided into two groups according to the timing of PBM therapy. Each group consisted of 40 patients. The first group received PBM therapy immediately after extraction and on the 3rd day after extraction. Group two received the PBM therapy on the 1st and 4th days postoperatively. Diode was the laser of choice because it has been reported to be effective at reducing postoperative trismus and swelling after extraction of the lower third molar.[11] The laser wand was applied by the surgeon extraorally at the insertion of the masseter muscle on the same side of the extraction as per the protocol of Aras et al.[12] A 4 W laser beam with a 2.8 cm^2 spot size emitting radiation continuously at a wavelength of 830 nm was used. Each application lasted 2 min (120 sec) so that each patient received ~ 171 J of energy per treatment. This higher dose of PBM therapy was necessary because the application was extraoral rather than direct on the extraction socket.

At each postoperative appointment, pain was assessed quantitatively by recording the number of analgesic tablets consumed daily as described by Sisk et al.[3] Six tablets indicated severe pain, four to five tablets indicated moderate pain, and two to three tablets indicated mild pain, whereas no tablets were consistent with no pain. To quantify the amount of trismus, the maximum interincisal distance between the maxillary and mandibular incisors was measured using a graduated Vernier scale. The measurements were taken in replicas of three before the local anesthetic administration preoperatively and at each postoperative appointment. Mouth opening limitation was then assessed according to the following equation:

$$\frac{\textit{postoperative mouth opening} - \textit{preoperative mouth opening}}{\textit{preoperative mouth opening}} \times 100$$

Facial swelling was assessed according to the method of Bello et al.[13] Measurements were made between three fixed points on the patient's face: angle of the mouth, angle of the mandible, and ear lobule. The measurements were made before the local anesthetic on the day of the procedure and at every appointment during the 1st postoperative week.

Statistical analysis was performed using the SAS software version 9.1 (SAS Institute Inc., Cary, NC). Descriptive statistics were performed for the demographic data. Two-way analysis of variance (ANOVA) was the method of choice. The null hypothesis was rejected when the p value was < 0.05.

Results

The 80 subjects ranged in age from 18 to 30 years with a mean of 24 years. Gender distribution was as follows: 48 female subjects (60%) and 32 male subjects (40%) with a ratio of 3:2. Pain experienced by the delayed treatment and immediate treatment groups is compared in Fig. 1 as the

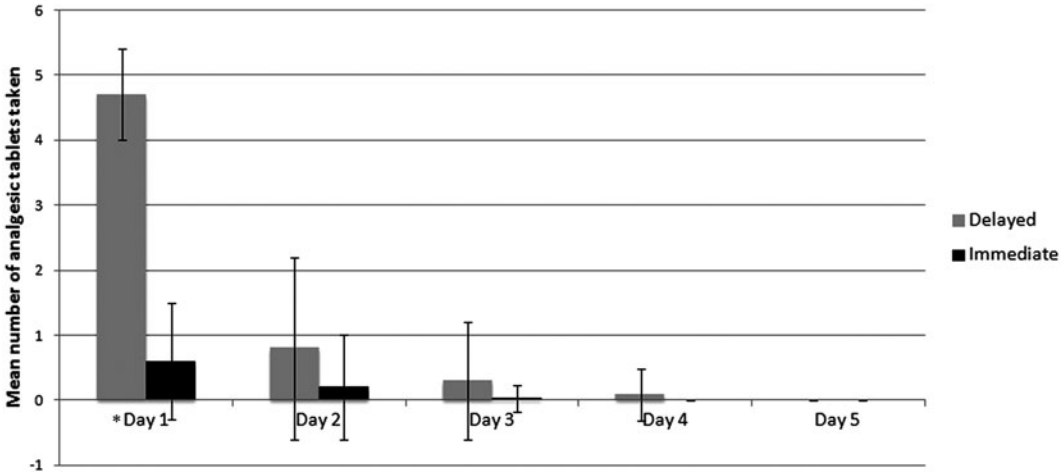

FIG. 1. Difference in mean number of analgesic tablets consumed per day by both the delayed and immediate treatment groups. The error bars represent the standard deviation (SD). The statistically significant results are highlighted with*.

mean number of analgesic tablets consumed per day. The subjects who received immediate PBM therapy experienced less pain than the delayed treatment group of subjects, as was evident by the difference in the mean number of consumed analgesic tablets. The difference between the two groups was statistically significant at the 5% level ($p < 0.05$), where $F = 201.97$ ($df = 1.39$).

Trismus for the delayed treatment and immediate treatment groups was compared as the percentage of limited mouth openings. The subjects who received immediate PBM therapy experienced less trismus than the delayed group of subjects, as evidenced by the difference in the mean percentage of limited mouth opening (Fig. 2). The difference between the two groups was statistically significant at the 5% level ($p < 0.05$), where $F = 352$ ($df = 1.47$).

Facial swelling for the delayed treatment and immediate treatment groups was compared as the percentage increase in the measured facial surface area. The subjects who received immediate PBM therapy experienced less facial edema than the delayed treatment group (Fig. 3). The difference between the two groups was statistically significant at the 5% level ($p < 0.05$), where $F = 338.25$ ($df = 1.55$).

Discussion

The three most commonly reported complications following the surgical removal of impacted wisdom teeth are pain, trismus, and facial swelling. For years, clinicians and researchers have tried to investigate techniques and methods to reduce these common complications. Gentle surgical approaches were advocated, medications were prescribed, and the use of laser therapy was investigated. The analgesic effect of PBM therapy is attributed to its ability to suppress the activity of the small superficial peripheral unmyelinated Aδ and C nerve fibers, collectively known as nociceptors, which are responsible for mediating pain and inflammation.[14] Suppressing the activity of the nociceptors also suppresses the release of bradykinin, thus reducing neural inflammation.[14] Moreover, there is evidence that PBM therapy can increase the levels of β-endorphin (β-ep).[15] Increased levels of β-ep are known to suppress the release of substance P from neurons, which in turn affects the neurons' ability to relay pain signals from the peripheral to the central nervous system.[15] Furthermore, PBM therapy reduces muscle spasm, which in turn reduces trismus.[12] Other reported effects of

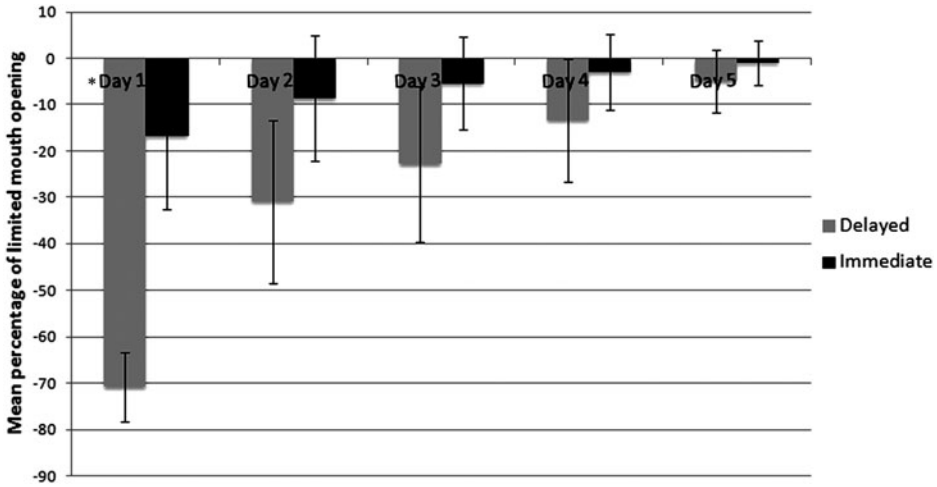

FIG. 2. Difference in mean percentage of limited mouth opening per day for both delayed and immediate treatment groups. The error bars represent the standard deviation (SD). The statistically significant results are highlighted with an asterisk (*).

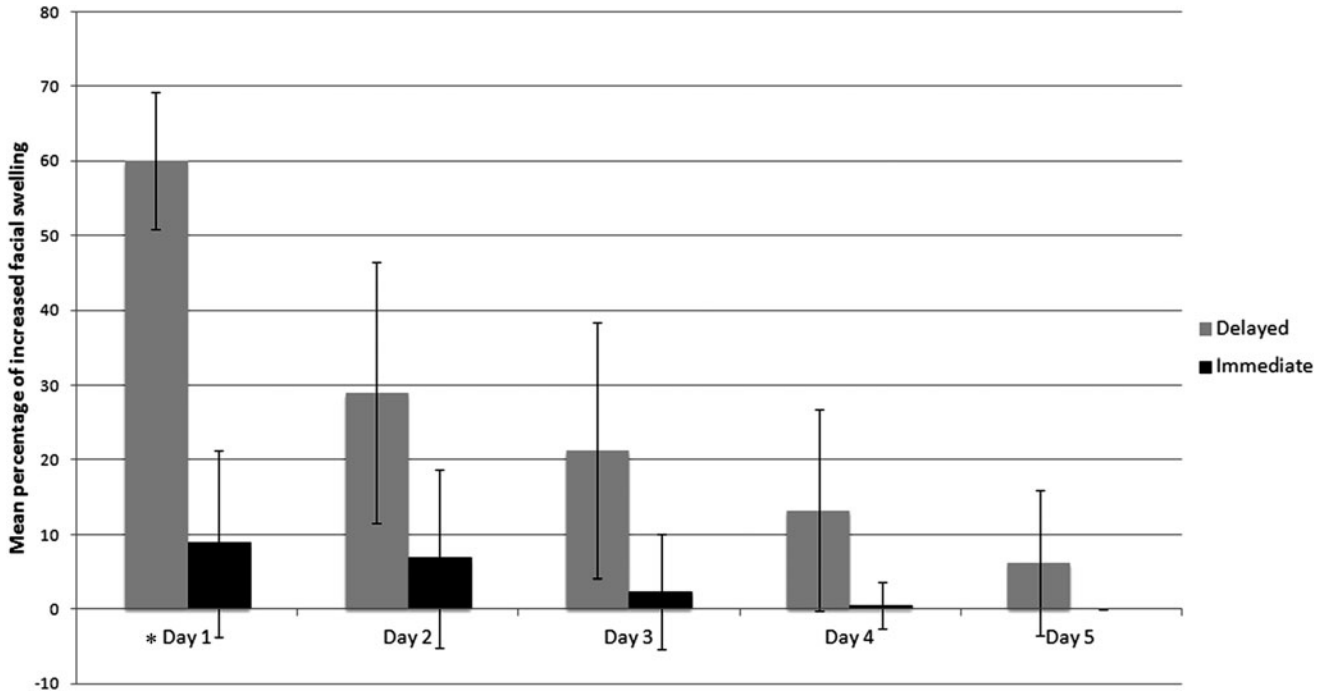

FIG. 3. Difference in mean percentage of increased facial surface area by both delayed and immediate group subjects. The error bars represent the standard deviation (SD). The statistically significant results are highlighted with an asterisk (*).

PBM therapy include increasing phagocytosis, increasing blood circulation, increasing the number and diameter of the lymphatic vessels, and suppressing the immune system,[16,17] all of which can help reduce the amount and severity of swelling following surgical manipulation.[17]

Most studies that have investigated the effect of PBM therapy on reducing postoperative complications were randomized clinical trials. Some investigated the effect of PBM therapy on only one of the three common complications, whereas many investigated the effect on all three complications. Recent studies show a promising positive effect of PBM therapy on reducing pain and swelling.[18,19] However, some studies continue to demonstrate no significant effect of PBM therapy on reducing pain, trismus, or swelling.[20]

Systematic reviews and meta-analyses have been undertaken to elucidate the benefit of PBM therapy following third molar surgery. Interestingly, the two most recent ones reached different conclusions. In 2012, a meta-analysis by Brignardello-Petersen et al. concluded that low-level laser energy irradiation had no benefit on pain or swelling, and only a moderate benefit in reducing trismus.[17] Later in 2014, another meta-analysis by He et al. concluded that lower laser therapy was efficacious at reducing pain, trismus, and swelling.[21] Authors of both systematic reviews were quick to point out that a comparison among studies was difficult because of the great variability in the type, energy, and application of the laser therapy. In addition, the assessment methods varied widely among studies. In the current study, every effort was made to keep the assessment methods objective and clear, hence choosing the number of analgesic pills consumed per day over the visual analog scale (VAS) for the assessment of postoperative pain. Nevertheless, we acknowledge that despite our best efforts, our assessment of facial swelling remains somewhat subjective, and we hope to develop a more objective means of measuring facial swelling in the near future.

More importantly, the number and timing of PBM treatments varied greatly among the studies. Some studies administered the treatment once, whereas others administered it several times. Some treatments were delivered before suturing, whereas others were delivered 3 days after surgery. More standardized trials are needed in order to reach a final conclusion regarding this matter, but our study was an attempt to isolate the variable of treatment timing and examine its effects, while keeping all other variables constant.

Future studies should also investigate the biphasic dose response to PBM therapy in humans, and examine the effect of irradiance time (fluence) to develop an optimal PBM therapy protocol for reduction of inflammatory complications following third molar extraction surgery. The biphasic dose response of PBM therapy has been long observed in many *in vitro* and animal studies, and more recent studies have given insight into the mechanism of this response.[22] It is now believed that a short fluence produces ''good'' reactive oxygen species (ROS), which through a sequence of events leads to cell proliferation and survival.[22] Production of ROS decreases as fluence increases up to a certain point, after which there is a second peak in ''bad'' ROS resulting in apoptosis of the cells.[22] This mechanism explains the observed Arndt–Schulz curve, which illustrates how too much power or fluence can actually inhibit rather than stimulate cell repair and proliferation.[22] Therefore, more studies are needed to formulate the optimal balance of power and time to produce the most beneficial effects.

Conclusions

To our knowledge, the current study is the first to investigate the difference between immediate and delayed

application of PBM therapy on pain, trismus, and swelling following the surgical removal of impacted mandibular third molars. The results demonstrate that PBM therapy is effective at reducing all three inflammatory complications when administered immediately following the surgical procedure. This effect is especially evident on the 1st day following surgery. Therefore, we advocate the immediate application of PBM therapy following odontectomy of impacted mandibular third molars.

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Compliance with Ethical Standards

All human studies have been approved by the appropriate ethics committee, and have, therefore, been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All persons gave their informed consent prior to their inclusion in the study.

Author Disclosure Statement

No competing financial interests exist.

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