Systematic Review of Orthodontic Treatment Management with Photobiomodulation Therapy

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Abstract

Objective: This systematic review of published research evaluates the parameters and reported outcomes in photobiomodulation therapies (PBMTs) used in management of pain and accelerated tooth movement during orthodontic treatment.

Background: Consequent to positive *in vitro* and animal studies, there has been considerable interest in the potential applications of PBMT to ameliorate pain and to accelerate orthodontic tooth movement. Due to the lack of consistency of wavelengths and parameters applied, there is as yet no consensus in respect of guidance for clinical use. Within the limitations of the reported literature, a digest of key outcomes and parameters is presented here to assist researchers and interested clinicians.

Materials and methods: Search engines, PubMed, Google Scholar, and Cochrane, were applied to identify clinical investigations into the potential benefits of PBMTs in orthodontic management. Keywords used were “low-level laser therapy,” “low-level light therapy,” “photobiomodulation,” “orthodontics,” “pain,” “tooth movement,” and “randomized clinical trial ≥5 years.” A total of 35 articles were identified, covering the 5-year period January 2013 to December 2018. Only human clinical trials were considered. Seventeen articles were included in this investigation and the reported parameters and outcomes were assessed and presented for comparison.

Results: Seven of nine studies supported the effectiveness of PBMT to reduce or prevent pain. There was no consensus on choice of wavelength and a range of parameters were found beneficial. Of the seven tooth movement studies included, four of the seven were positive, of which two used a home-use light-emitting diode (LED) device, as opposed to a clinician-applied laser. A variety of wavelengths and parameters were found to be effective in accelerating tooth movement in the range of 20–40% compared with control.

Conclusions: Due to a lack of consistency in approach, further studies are required to achieve a high level of acceptance. The clinical logistics associated with frequent applications supports the concept of patient home delivery use of LED devices, although there are insufficient studies at present to make an evidence-based determination of this type of appliance. To gain more general professional acceptance of the use of PBMT in orthodontics, a continued effort to extend the number of quality human clinical trials is required. Based on the current evidence base, further positive onward progression can be regarded as inevitable.

Keywords: photobiomodulation (PBM), low-level laser therapy, low-level light therapy, light emitting diode, pain/pain management, orthodontic tooth acceleration, orthodontic pain, systematic review

Introduction

THE ADJUNCTIVE USE of lasers and light-emitting diode (LED) devices as phototherapy tools to assist in orthodontic treatment management has been the subject of many scientific *in vitro*, *in vivo* animal, and more

recently human clinical studies.¹ The review of published articles presented here relates to the possible use of photobiomodulation therapy (PBMT) to alleviate pain associated with orthodontic tooth movement (OTM). In addition, there is considerable interest in the potential for the acceleration of OTM.

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A typical course of orthodontic treatment can take between 12 and 24 months to complete with a variable period of post-treatment time for retention with appliances or fixed splints. Pain associated with standard orthodontic treatment is a common and significant problem. Other complications of therapy include alveolar bone resorption, root resorption, caries, and periodontal issues, as well as rapid relapse after treatment if retainers are not used. These issues represent a significant problem associated with reduced patient compliance and a reduced uptake in acceptance of treatment.²⁻⁹

Given the rise in demand for treatment and in recognition of the barriers to acceptance of therapy, there has been considerable clinical interest reflected in the current scientific literature in respect of the integration of PBMT into pain management, to accelerate OTM, and to increase the rate and quality of bone remodeling.¹⁰

Orthodontic treatment with or without surgery to achieve arch relationship correction and/or tooth movement frequently has several disadvantages, the prime of which may be transient pain and/or pathological (nonphysiological) changes in tooth root structure (resorption) and the supporting alveolus, caused by excessive loading forces applied during active therapy.¹¹⁻¹³

It is necessary to consider the rigor required in developing the positive association of photobiomodulation (PBM) and its adjunctive role in active orthodontic treatment. A null hypothesis exists to acknowledge the existence of doubt in some minds—effectively, PBMT has not been shown to provide added benefits during orthodontic treatment. The simple reporting on published studies in providing a narrative review would not allow the development of consensus, and as such, this review has followed a structured (systematic) format to allow the null hypothesis to be considered further in the light of the examination of randomized clinical studies.

Clinical Applications of PBMT in Orthodontics

The use of laser PBMT adjunctive to active orthodontic treatment, to modulate pain response, and to encourage the response of the alveolar bone to facilitate tooth movement or maxillary expansion has developed during the past 20 years.

Two essential areas can be identified:

- (i) PBMT—pain modulation (improved patient compliance)
- (ii) PBMT—accelerated rates of tooth movement (shorter treatment times)

PBMT: pain modulation

Keywords used were photobiomodulation, low-level laser therapy, “low-level light therapy,” orthodontics, pain, and randomized clinical trial ≥ 5 years. Seven recent publications demonstrate a positive relationship between pain and PBMT.¹⁴⁻²⁰

Additionally, some articles are included, which satisfy the inclusion criteria, but demonstrate either a null outcome or a result that failed to achieve statistical significance.^{21,22}

PBMT: accelerated rates of tooth movement

PubMed was used to identify randomized, controlled clinical trials during the past 5 years; published articles provide a

positive relationship between PBMT and expedited/accelerated tooth movement during appliance therapy.²³⁻²⁶ Keywords used were photobiomodulation, low-level laser therapy, “low-level light therapy,” orthodontics, tooth movement, and randomized clinical trial ≥ 5 years.

In addition, some articles cited satisfy the inclusion criteria, but demonstrate either a null outcome or a result that failed to achieve statistical significance (Fig. 1).^{22,27,28}

Outcome and Analysis

Pain studies

There is agreement in the literature that a single applied dose at the time of active loading can be effective in respect of pain management. Current concepts in the mechanisms of PBMT and pain are still evolving; however, in view of the multiple supportive clinical studies, it is reasonable to consider PBMT as a supportive measure in orthodontics. Although there is variation in applied wavelength and irradiance, a trend is apparent that PBMT pain management can be an effective measure.

The range of laser emission wavelengths commonly employed in pain management in the literature is from 632.8 to 910 nm. Given the wider range of wavelengths used in other published studies for laser analgesia applications, it

FIG. 1. PRISMA selection criteria. PRISMA chart of published articles relating to orthodontic tooth movement, PBM, and pain assessment. PBM, photobiomodulation.

cannot be concluded that the only effective wavelengths are within this narrower range. The majority of published literature records laser wavelengths that fall within the so-called near-infrared (NIR) optical window.²⁹ A coherent laser source in the 650–1150 nm band is relatively poorly absorbed and is associated with a high degree of scattering.³⁰ This in turn can lead to increased optical transmission due to deep tissue photon collision and amplification (speckles). It is possible that optical sources with a wider bandwidth may have reduced optical penetration, which may impair the capacity of the LED-type device to work well in PBMT pain management.³¹ Given the evident multiphasic response of biological tissues to light, it is apparent that the dosimetry associated with pain management is in a range higher and perhaps wider than that associated with accelerated tooth movement and bone augmentation.

In the studies that recorded more positive outcomes, there is no consistent wavelength, dose (J), radiant exposure (J/cm^2), irradiance (W/cm^2), tip diameter, average power output, peak power (for gated mode), time, or position of the points of application. It is, however, noteworthy that the radiant exposure ranged from $12 \text{ J}/\text{cm}^2$ up to $183 \text{ J}/\text{cm}^2$. In addition, the average power output ranged from 10 mW through to 160 mW with a delivered dose of 5–18 J/tooth. Further, the irradiance ranged from 0.05 to $3.5 \text{ W}/\text{cm}^2$. In all the successful clinical trials, the laser tip was placed on either side of the crown of the tooth as well as, in two studies, at the apical area (Table 1).

OTM studies

Of the seven studies included, four demonstrated a positive outcome with increases of 20–40% in the rate of OTM. Of the positive studies, two used NIR 808–830 nm diode lasers and two applied patient home-use, extraoral (visible to NIR 618–850 nm) LED devices. In the laser groups, radiant exposure ranged from 0.71 to $5 \text{ J}/\text{cm}^2$. In addition, the average power output ranged from 20 to 200 mW with a delivered dose of 2–8 J/tooth. Within the confines of the data reported, the laser studies used spot sizes in the range of $0.04\text{--}0.28 \text{ cm}^2$ with an irradiance in the range of $0.48\text{--}0.71 \text{ W}/\text{cm}^2$, delivering radiant exposures ranging from 2.25 to $7.1 \text{ J}/\text{cm}^2$. In both studies, the apices were irradiated along with two to eight additional points on various sites of the length of the tooth with frequent treatments (Table 2).

Discussion

PBMT: dosimetry relative to fluence homogeneity

Laser dose may be seen as a product of applied radiant energy exposure, frequency, and timing of application, as well as the anatomical site application relative to 2D and 3D planes. Further, the rate of energy delivery as well as power density may influence clinical outcomes.^{32–35}

A current area of interest centers on the emerging significance of uniformity and homogeneity of the spot size. There do not appear to be any published, peer-reviewed, randomized, clinical trial articles to allow an investigation of the significance of flat-top fluence in comparison with Gaussian X-section beam distribution.^{36,37}

The delivery of consistent, dose–response coherent photonics that are matched to the target tissue remains a chal-

lenge for the clinician. Over recent years and with increasing investigation, a shift has emerged to recognize the distinct and fundamental difference between control panel laser parameters and the fluence value consequent upon energy delivered and surface configuration of the laser beam. Together with site specificity of a variable anatomical target and variations in dose repetition along with the other delivery variables as described above, a consistent and reliable outcome of dose related to response can pose a clinical challenge.^{1,32,36}

Anatomical variance may be due to the soft tissue biotype overlying the target area, cutaneous pigmentation, osseous density and structural elements (cortical vs. trabecular bone), and the position of the tooth within the sagittal and horizontal planes. The consequent variable range of scatter and penetration of the NIR photon beam may compromise a fixed set of laser operating parameters.³⁰

The susceptibility of target cellular elements to variation in dose has been reported as being moderately wide and this may be expressed in terms of beam energy cross-sectional analysis, trans-alveolar power diffusion, and treatment repetition.^{37–40}

Considerable power losses may occur in deep tissue irradiation, amounting to orders of 90% through as little depth as 5 mm.^{29,41,42} This will have an effect on the surface dose required to maximize the therapeutic dose delivered to osseous cells and is further compounded by the dangers of dose choice when using Gaussian beam delivery. It is recognized that there is a therapeutic dose window for photobiostimulation in the range of around $2\text{--}8 \text{ J}/\text{cm}^2$ beyond which there is progressive photobioinhibition.^{43,44} Given the difficulty of reliably delivering an optimized dose at depth, it is proposed here that an average dose at a target tissue level of $5\text{--}6 \text{ J}/\text{cm}^2$ be employed as this permits variance in actual delivered dose of around 50% while still falling into the therapeutic range for optimization of cellular and tissue responses.

Treatment repetition

Treatment repetition times and optimization of consistent, positive cellular stimulation through PBMT will be significantly affected through the type and turnover rate of the target cell strain and overall by patient availability. All of the studies related to accelerated OTM use multiple applications and given the diversity of methods employed in the literature to date, it is not possible to offer an evidence-based determination as to the optimum timing and frequency of the same.

PBMT: pain modulation

The mechanisms of PBMT are the subject of continued research to optimize clinical outcome. Although it is apparent that there are sustained, evidence-based clinical applications in relation to pain management, the underlying cellular and tissue responses to PBMT are still being investigated.⁴⁵ Most recently, a number of theories have been proposed that may offer additional insight into the phototransduction processes associated with laser-induced analgesia.^{46,47} Pending continued research to further elucidate the best standardized approach, it is apparent that higher range dosimetry is associated with an improved clinical result in PBM-assisted pain management.⁴⁸ The result of this

TABLE 1. PHOTOBIO-MODULATION THERAPY ADJUNCTIVE TO ORTHODONTIC THERAPY: PAIN MODULATION

Article (ref. no.)	Subjects	Study design (laser/ placebo/control)	Pain measurement	Wavelength and power	Dose
40 (Dominguez et al. ¹⁴)	60/60	Single-blind RCT (split mouth)	VAS	830 nm GaAlAs 100 mW	Spot size: 0.06 cm ² 80 J/cm ² 2.2 J buccal and lingual
42 (Nobrega et al. ¹⁵)	30/30	Double-blind RCT	VAS	830 nm AlGaAs 40.6 mW	Spot size: 0.13 cm ² 5 points/tooth 1 J/point 5 J/tooth
43 (Abtahi et al. ¹⁷)	29/29	Single-blind RCT (split mouth)	VAS	904 nm GaAs 200 mW	Spot size: 0.4 cm ² 6 J/tooth 2 points
47 (Herravi et al. ²²)	20/20	Single-blind CCT (split mouth)	VAS	810 nm GaAlAs 200 mW	Spot size: 0.28 cm ² 11 doses 21.4 J/cm ² /point 10 points
41 (Eslamian et al. ¹⁶)	37/37	Double-blind RCT (split mouth)	VAS	810 nm GaAlAs 100 mW	10 doses (2 J/cm ² , 20 sec) buccal (cervical third of roots) for distal and mesial of second premolars and first molars (five doses). Repeat for lingual (five doses).
44 (Sobouti et al. ¹⁸)	27	RCT (split mouth) placebo control	VAS	632.8 nm He-Ne 10 mW	6 J/cm ² tip 5 mm diameter
46 (Marini et al. ¹⁹)	40/40/40	Double-blind RCT laser/placebo/ control (upper and lower)	VAS	910 nm GaAs 160 mW	Spot size 0.5 cm ² . Gated CW—30 kHz/duty cycle of 80% (4:1 on/off). Buccal and lingual 18 J/cm ² each tooth
45 (Farias et al. ²⁰)	15/15	Double-blind RCT (split mouth)	VAS	810 nm GaAlAs 100 mW	Spot size 0.28 cm ² Fluence 2 J/cm ² per point. Mesial, distal, and apical. 6 J/cm ² each tooth
48 (Martins et al. ²¹)	31/31	Double-blind RCT (split mouth)	VAS	830 nm Laser 100 mW	Spot size 0.03 cm ² 95 J/cm ² 8 sites: 2 mesial/2 distal interproximally on the buccal and lingual. 30 sec per application—24 J/molar

CW, continuous wave; RCT, randomized clinical trial; VAS, variable analogue scale.

TABLE 2. PHOTOBIMODULATION THERAPY ADJUNCTIVE TO ORTHODONTIC THERAPY: TOOTH MOVEMENT

Article (ref. no.)	Subjects	Study design (laser/ placebo/control)	Laser wavelength	Power and time	Dose (J/cm ²)	Total energy
29 (Genc et al. ²³)	27	Split mouth plus 7 -ve control	Diode laser 808 nm	200 mW 10 sec 0.28 cm ²	0.71/point 7.1/session	0.2/point 2.0/session
47 (Herravi et al. ²²)	20	Spilt-mouth RCT	Diode laser 810 nm	200 mW 30 sec 0.28 cm ²	21.4 J 10/session	6 J/point 60 J Null
35 (Chung et al. ²⁷)	11	Spilt-mouth RCT	LED 850 nm	150 mW/cm ² 21 min/day	189 J/cm ² extraoral illumination	0.92–6.92 J/cm ² Null
32 (Ekizer et al. ²⁶)	20	Spilt-mouth RCT	LED 618 nm	CW 20 mW/cm ²	No computed fluence values Extraoral illumination	24 J/cm ²
36 (Yassaei et al. ²⁸)	11	Spilt-mouth RCT	Diode laser 980 nm	100 mW 56 sec	No computed fluence values extraoral illumination	No computed fluence spot size unknown Null
31 (Nahas et al. ²⁵)	40	Parallel RCT	LED 850 nm	90 mW/cm ² 20 min/day	108 J/cm ² extraoral illumination	Fluence 12 J/cm ²
30 (AlSayed Hasan et al. ²⁴)	26	Parallel RCT	Diode laser 830 nm	CW 150 mW 15 sec per point	Fluence 2.25 J/cm ²	2 J/point. Four points (2 buccal/2 lingual)

LED, light-emitting diode.

review is consistent with PBMT being accepted as an evidenced-based approach for orthodontic pain management.

It is emphasized that the most successful clinical trials involved applications at multiple points at the apices and around the crown of the tooth, and the dose described in the studies included here is of the sum total of applied energy in the range of 5–18 J/tooth. High-dose regimens can be the trigger for phototoxicity,⁴⁹ and it is suggested here that within the limitations of the current evidence base, a safe range for therapeutic exposure be kept to 10–30 J/cm² at a low-power output and an irradiance of less than 500 mW/cm². These limits are, however, offered as representing safe boundaries rather than being rigidly prescriptive.

PBMT: accelerated OTM

Studies conducted in animal models have shown promise that laser and LED phototherapy can improve OTM. Measures applied in animal studies have included histology assessing bone density and volume, proliferation of osteoclasts and osteoblasts, the number of capillaries, and changes in the number of inflammatory cells. By using monoclonal antibodies, there have been measurements of immunohistochemical staining of important cytokines involved in bone remodeling, such as osteoprotegerin and the receptor activator of nuclear factor kappa-B ligand. Animal studies showed that application of lasers in wavelengths of 650–940 nm increased the rate of tooth movement two to three times compared with control groups. In addition, this outcome was supported by histological evidence of increased cellular activity and significant signs of an increase in bone remodeling compared with the controls. Animal studies represent a substantial body of evidence-based research. There is no agreement, however, on laser or LED wavelengths, duration of treatment, frequency of treatment, energy density applied, or total dose (fluence). Faced with a heterogeneous set of experimental studies based on a variety of animal models, it is not possible to extrapolate the results to human subjects.^{50–57}

The majority of human studies demonstrate a positive benefit and it could be considered that the treatment is seen as passing the threshold as an evidenced-based approach. Given the heterogeneous wavelengths and parameters employed in the limited number of studies accepted for inclusion, it is premature to offer a protocol to guide clinicians. An examination of published data, using the CONSORT criteria of choice refinement, offers an opportunity to examine the adjunctive benefits of PBMT within orthodontic treatment on several levels. As has been stated already, the diverse range of parameters within the many published studies has provided a challenge that would mitigate against the validity of a meta-analysis; however, it has allowed a structured consideration of results and their interpretation to fulfill the objectives of a systematic review.

In respect of home-use, transdermal LED appliances, due to considerable variation in tissue thickness plus the presence of multiple layers of keratinized epithelium, this approach must be regarded with caution. A more recent type of intraoral LED home appliance is available, although this approach has not as yet satisfied the requirements for inclusion in the accepted evidence base. This type of device does, however, offer some potentially useful features as it

overcomes a logistical problem for prescribing clinicians. It is hoped that this newer intraoral device may be subject to future well-designed and constructed clinical trials.⁵⁸

Conclusions

The use of lasers and LED devices has been subject to a considerable degree of interest, as reflected in the volume of the evidence-based literature. In respect of the management of pain associated with OTM, this appears to be a useful, emerging clinical measure. Due to a lack of consistency in approach, further studies are required to achieve a high level of acceptance. Based on the current evidence, further onward progression can be regarded as inevitable. In respect of the use of lasers and LED devices for OTM, although there is considerable supportive literature from animal and *in vitro* studies, there is the need for further studies to permit offering a formal protocol at this stage. Applying the strict criteria of CONSORT and the PRISMA statement to attain a high level of acceptance to the required level for a future systematic review and meta-analysis will demand more quality research as a prequel to general professional acceptance of this novel approach.

Through examination of available peer-reviewed data, notwithstanding the range of laser operating parameters, it is possible to conclude that on a balance of probabilities, there is a multi-factorial benefit to be derived through the adjunctive use of PBMT in clinical orthodontics; from this, it is possible to discount the null hypothesis.

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