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Review Article **Orthodontics**

Efficacy of Photobiomodulation in Orthodontic Pain Management: A Systematic Review of Literature

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Abstract

***Aim and Background*:** This systematic review aimed to investigate the efficacy of photobiomodulation (PBM) on alleviating orthodontic pain. ***Review Methods*:** An extensive electronic search for randomized control trials via Medline (via PubMed), The Cochrane Controlled Clinical Trials Register, and Science Direct up to October 15, 2023 was done. Hand searching was performed for relevant journals. Reference articles were retrieved and exported to Zotero software. The risk of bias was assessed using Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2). ***Results*:** A total of 8 articles were considered for systematic review. Most of the studies arrived at the consensus that photobiomodulation (PBM) indeed reduces the pain associated with orthodontic treatments. ***Conclusion*:** The synthesis of available evidence in our analysis reveals a substantial body of research suggesting a positive effect of PBM on reducing orthodontic pain. However, the existing variations in PBM parameters, and outcome measurements emphasize the necessity for more standardized approaches in future investigations.

Keywords: Laser, Systematic Review, Pain, Orthodontic, Photobiomodulation.

1. INTRODUCTION

Photobiomodulation therapy (PBM) is emerging as a promising approach to enhance the orthodontic experience by addressing some of the challenges commonly associated with traditional orthodontic treatments. Although orthodontics is a highly effective method for correcting malocclusions and improving dental alignment, the process often involves lengthy treatment times [1], and significant discomfort, making it a daunting experience for many patients [2]. PBM, a non-invasive therapy that utilizes targeted light energy, has gained considerable attention over recent years for its potential to alleviate pain, accelerate tissue healing, and generally improve patient comfort. The mechanism behind PBM lies in its use of specific wavelengths of light, which are applied to the affected areas, leading to modulation of cellular processes that can reduce inflammation, promote tissue regeneration, and encourage faster healing [3]. Within the context of orthodontics, PBM offers promising possibilities for mitigating the pain often experienced during tooth movement and potentially shortening the overall treatment duration. In an effort to thoroughly assess the efficacy and broader applications of PBM in orthodontic treatment, researchers have conducted numerous studies across various settings, including in vitro experiments, animal models, and human clinical trials. These studies have examined the impact of PBM on a range of orthodontic outcomes, such as pain relief, acceleration of tooth movement, and prevention of complications like root resorption. This systematic review aims to synthesize the available research on PBM's role in orthodontics, particularly its capacity to manage pain. Ultimately, the goal is to determine whether PBM can be effectively integrated into orthodontic treatment protocols, thereby providing a more comfortable and efficient experience for patients undergoing orthodontic care.

2. MATERIALS AND METHODS

2.1. Protocol and Registration:

The Cochrane Handbook for Systematic Reviews of Interventions mentioned using the PICOS

framework as a model for developing a review question, thus ensures that the relevant components of the question are well defined.

The eligibility criteria of this review followed the PICOS criteria as such:

- ✓ **Population** = Orthodontic patients receiving photobiomodulation therapy (PBM).
- ✓ **Intervention** = PBM used as an aid intervention in fixed orthodontic treatment.
- ✓ **Compared with** = Control groups receiving fixed orthodontic treatment without any other interventions and/or placebo group receiving simulated PBM treatment.
- ✓ **Outcome of interest** = pain score perception
- ✓ **Study type** = Randomized controlled clinical trial (parallel group or split mouth design).

2.1.1. Inclusion Criteria:

The included articles met the following criteria:

- ✓ Articles in English dating from 01/01/2017 to 15/10/2023.
- ✓ The articles must meet all PICOS criteria with the design of randomized clinical trials (RCTs) conducted on humans (parallel group or split mouth design).
- ✓ Human teeth subjected to orthodontic force application in any direction.
- ✓ PBM interventions conducted with LEDs or LLLs equipment.
- ✓ Studies presenting the parameters of PBM and the individual characteristics of patients.
- ✓ Outcome variables were defined as Overall treatment time, orthodontic tooth movement rate (tooth displacement in a determined period of time), pain score perception, orthodontic root resorption crater volume.

2.1.2. Exclusion Criteria:

- ✓ Non-randomized clinical trials
- ✓ In-vitro studies or animal studies
- ✓ Studies without a control/comparison group
- ✓ Review articles, case reports, case series, and letters to editor.
- ✓ Studies available only in languages other than English.
- ✓ Studies that included fewer than 10 patient or hemiarch (quadrant) per group.
- ✓ Patients of studies exposed to previous orthodontic treatment.
- ✓ Studies involving participants suffering from metabolic disorders, or taking medications impeding or hastening tooth movement.
- ✓ Studies involving participants who had a high caries index or periodontal disease.
- ✓ Studies that used high-level laser or red laser.

2.2. Information Sources and Search Strategy

The review authors performed an extensive electronic search for randomized controlled trials realized on humans up to October 15, 2023, in three databases: PubMed, Science Direct, and Cochrane Library. The search strategies employed are outlined in Table 1.

Table I: search strategies in the three databases

Database	Search strategy
PubMed	("low-level laser" OR "low-level laser therapy" OR photobiomodulation) AND orthodontic* AND pain
ScienceDirect	("low-level laser" OR "low-level laser therapy" OR photobiomodulation) AND orthodontic AND pain
Cochrane Library	("low-level laser" OR "low-level laser therapy" OR photobiomodulation) AND orthodontic* AND pain

All articles and manuscripts published in English or with English translations available were incorporated in the search and only articles published from 01-01-2017 were selected. The search was complemented by a manual review of the references of the studies included.

2.3. Data Extraction

Titles and abstracts were selected independently by the investigators to verify their eligibility. In cases of discrepancy, consensus was obtained by discussion. The same reviewers then examined the references that appeared to meet the inclusion criteria in their entirety.

The information regarding the selected studies was recorded using three data extraction forms specifically created for this purpose to systematically and uniformly analyze and compare each selected article.

A first form for the extraction of the following data: author and date, total number of patients / Teeth ,number of subjects in PBM group, number of subjects in control group, mean age of patients, the orthodontic mechanics and the clinical assessement used in the trial, and the principal outcome of the trial.

A second form for the extraction of light parameters data: the equipement used, wavelength, irradiation points, dose of energy and the phototherapy session protocol.

A third and final form for the extraction of: the mean values of the main outcome, the results and the conclusion of each article.

Then, the gathered information was grouped and synthesized into tables for discussion and analysis to address the main question of the research.

2.4. Risk of Bias Assessment

The assessment of the risk of bias in the included studies was conducted using Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2). RoB 2 is the recommended tool for evaluating the risk of bias in randomized trials included in Cochrane Reviews [4]. The tool is organized into five domains that identify potential sources of bias in the study results, the five domains are:

1. Bias arising from the randomization process.
2. Bias due to deviations from intended interventions.
3. Bias due to missing outcome data.
4. Bias in the measurement of the outcome.
5. Bias in the selection of the reported result.

Within each domain, a set of questions known as 'signalling questions' is designed to gather information relevant to the risk of bias. An algorithm utilizes the responses to these questions to generate a proposed judgment regarding the risk of bias for each domain. This judgment can be categorized as 'Low' or 'High' risk of bias or expressed as 'Some concerns.' [4].

The reviewers independently assessed the risk of bias using an excel tool designed to implement RoB 2, and the differences between the reviewers were resolved by discussion.

2.5. Level of Evidence

The evaluation of the level of evidence was carried out utilizing the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) system by the two reviewers independently.

The GRADE system principles were applied to assess the overall quality of the body of evidence associated with the outcome. To facilitate this assessment, a "Summary of Findings" (SoF) table was constructed using the GRADEpro GDT software available at http://gdt.guidelinedevelopment.org.

The evaluation of the body of evidence considered factors such as the overall risk of bias in the included studies, directness of the evidence, inconsistency of results, precision of estimates, risk of publication bias, and the magnitude of the effect. Depending on the severity, the quality of evidence can be downgraded by one or two levels for each aspect. We categorized the quality of the body of evidence for each primary outcome as high, moderate, low, or very low.

3. RESULTS

3.1. Study Selection

The electronic search retrieved 527 results from all the databases.

451 results remained after removal of duplicates, which were then screened by titles and abstracts. 56 of those were of the desired study design. Six articles were not accessible for full text screening and 42 articles were excluded for not matching the eligibility criteria, which left us with a total of eight articles to be included in this systematic review.

A flowchart of the article selection process for each stage of the review is presented in Figure 1.

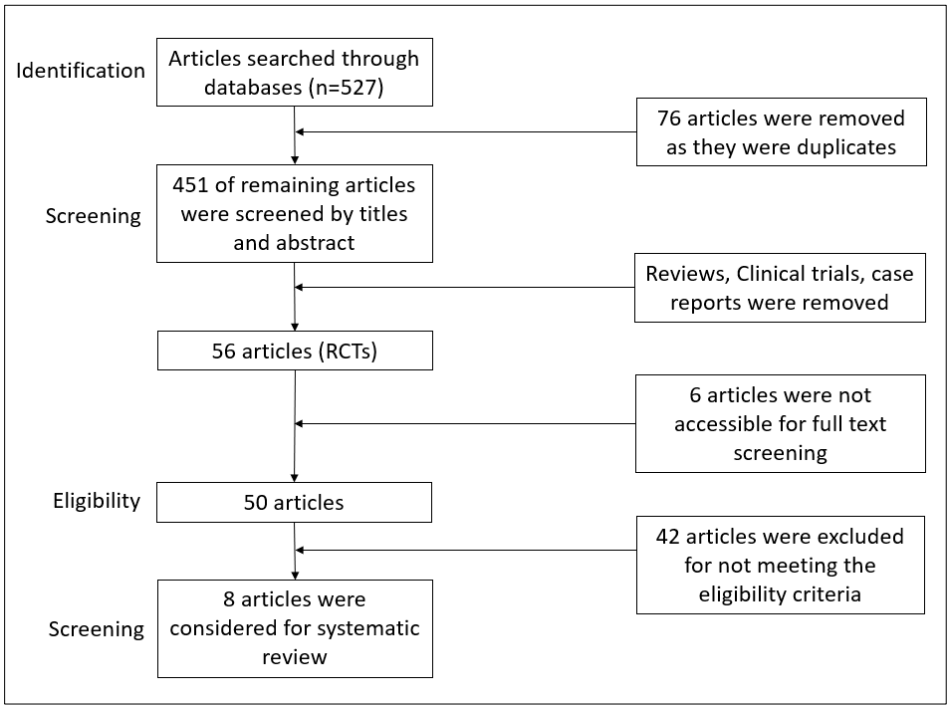

Figure 1: Flowchart of the article's selection process

1.1. Characteristics of Included Studies

Fourteen relevant publications assessing the effectiveness of PBM in orthodontic tooth movement pain management were identified as eligible according to the predefined inclusion criteria for this review.

The gathered data was grouped into the tables II, III and IV below:

Table II: Clinical characteristics of the RCTs exploring orthodontic pain reduction

Author and date	Patients / Teeth	Number in PBM group	Number in control group	Mean age	Orthodontic mechanics and clinical assessement	Outcome
Mohammad Moaffak A. AlSayed Hasan 2020 [5]	26 patients	13	13	20.07	For patients in both groups the first maxillary premolars were extracted, molars were banded, a 0.022 in. MBT prescription fixed orthodontic appliance was bonded and a 0.014 in. NiTi archwire was inserted and engaged to all maxillary teeth using ligature wires. In the laser group, a LLL irradiation was applied immediately after initial orthodontic archwire placement.	Patients were asked to score their pain degree after 1, 6, 24, 48, and 72 h of treatment application for both spontaneous and chewing pain.
Irfan Qamruddin *et al*., 2018 [6]	42 patients	42	42	19.81	The orthodontic treatment was commenced by bonding the maxillary arch with 0.022-inch slot MBT prescription brackets. Alignment and leveling was achieved using 0.012- in super-elastic nickel-titanium (NiTi) wire followed by 0.014, 0.016, and 0.018-in NiTi wires, changed at 4-week intervals between each wire. Laser therapy was applied on the experimental side afterplacement of each archwire.	Feedback for spontaneous pain and pain on mastication at consecutive 12 hours intervals for 7 days
Song Wu *et al*., 2018 [7]	40 patients	20	20	20.8	The arch wire (0.014 super plastic nickel-titanium arch wire) was placed in self-ligating brackets.	Perception of pain at 0 h, 2 h, 24 h, 4 d, and 7 d after the orthodontic forces were applied.
Prasad *et al*., 2019 [8]	20 patients	10	10	21.3	All the subjects were treated with appliance of standard 0.022 mclaughlin, bennett and trevisi prescriptions and had a passive 0.019×0.025 stainless-steel archwires as working wire. To each group, a retraction force of 200g/cm2 per side was applied to maxillary right and left quadrants using type 1 active tiebacks.	Perception of pain score
Sfondrini *et al*., 2020 [9]	26 patients	13	13	11,8	A clinician cemented two bands for each participant (3M, Unitek Molar Bands, Saint Paul, USA) on upper first molars for a multiband-multibracket orthodontic treatment.	Assessment of pain intensity at different time points: 5 minutes (T0), 1 hour (T1), 12 hours (T2), 24 hours (T3), and 72 hours (T4) after molar banding
Matys *et al*., 2019 [10]	76 patients	26	25	35.1	Orthodontic fixed appliances) that were used in the treatment of our patients had the following prescriptions: MBT, 0.018 slot. As initial arches, NiTI 0.014 was used.	Perception of pain score measured at 7 time points: 1 h, 6 h, 1 day, 2 days, 3 days, 4 days, and 5 days after the orthodontic appliance placement.

Nicotra *et al*., 2020 [11]	56 patients	19	20	12.03	The orthodontic device, i.e., maxillary expander or transpalatal arch, was inserted and cemented using fluoride cement. The appliance was kept passive, without applying active forces, up to the end of the time-line schedule, in order to avoid confounding factors that could have altered the perception of pain.	Perceived pain immediately after bands cementation, 6 h, 24 h, and from day 2 to day 5
Brito *et al*., 2022 [12]	54 patients	28	26		Non-extraction orthodontic treatment performed with the preadjusted fixed appliances, 0.022″ slot; installation of the 0.012″ thermoactivated nickel-titanium archwire as the beginning of the alignment and leveling phase	Level of pain

Table II: Phototherapy carachteristics of the RCTs exploring orthodontic pain reduction

Author and date	Equipement	Wave length	Irradiation points	Energy density per session	Laser session
Mohammad Moaffak A. AlSayed Hasan 2020 [5]	LLL device (CMS Dental ApS, 55 Wildersgade, 1408 Copenhagen K, Denmark)	830 nm	LLL was applied to each root of the six maxillary anterior teeth roots. Each root was divided to apical and cervical halves. The device tip was centered in each half with direct contact perpendicular to the oral mucosa from both the buccal and palatal sides so that each tooth receives four application points.	2 J per point 8 J / tooth	An application time of 15 s per point : the total application time was 6 min.
Irfan Qamruddin *et al*., 2018 [6]	Aluminum-gallium-arsenide (Al-Ga-As) diode laser	940 nm	The mucosa was irradiated for 3 seconds each on 5 points facially and palatally per tooth, starting from central incisor to the first molar. These points were mesial and distal over the cervical-third of the root and middle of the root, and mesial and distal over the apical-third of the root.	75 J per tooth	Laser therapy was applied on the experimental side after placement of each archwire.
Song Wu *et al*., 2018 [7]	Gallium-aluminium-arsenic diode laser	810-nm	LLLT was applied buccally and lingually to an upper canine at 6 points: mesial, distal, and at a site corresponding to the middle of the root of the canine tooth for 20 s each in the LG	2 J·cm-2	The LG received the (LLLT) immediately after (0h) the arch wire 0.014 NiTi was placed and then again at 2h, 24h, 4d, and 7d
Prasad *et al*., 2019 [8]	diode laser	980nm	On labial and palatal sides of each tooth in the arch	2.5 W/cm2	A single dose of LLLT
Sfondrini *et al*., 2020 [9]	diode laser, GaAlAs	830 ± 10 nm	The laser was applied in 4 points for each banded molar (2 mm apically from the gingival margin): on the mesiobuccal (MB), distobuccal (DB), mesiopalatal (MP), and distopalatal (DP) portions of the teeth	7.5 J/cm2	One session
Matys *et al*., 2019 [10]	diode laser	635-nm	23 points (irradiation on each tooth apex area and interdental papillae area from the maxillary right first molar to the maxillary left first molar), total time of the laser application was 1 min and 55 s.	1.59 W/cm2 total energy per session 46 J	One single session
Nicotra *et al*., 2020 [11]	AlGaAs diode laser emitting infrared radiation	980 nm	positioning the optical fiber tip over the first molar on both sides with a single spot application	30J/cm2 per tooth	The procedure was repeated 3 times at an interval of 10 s. One session

			moving the tip from vestibular toward the palatal side for 10 s		
Brito *et al*., 2022 [12]	gallium-aluminum-arsenide (GaAlAs) infrared laser	808 nm	from the distal region of the first molar to the distal region of the opposite first molar : three points between the roots and distal spaces of the first molar (cervical, middle, and apical) of the buccal and lingual/palatal sides were irradiated for 15 seconds, totaling 12 irradiations in each tooth.	26 J/cm2 (0.78 J) per point total energy of 9.36 J per tooth	The average time for irradiation of all teeth was 19.5 minutes. only once, immediately after brackets bonding and installation of the first archwire of the orthodontic treatment

Table IV: Findings of the RCTs exploring orthodontic pain reduction

Author and date	Evaluation method	Evaluation interval after start of orthodontic treatment	Results	Conclusion
Mohammad Moaffak A. AlSayed Hasan *et al*., 2020 [5]	Visual Analogue Scale (VAS) of 100	After 1, 6, 24, 48, and 72 h of treatment application	The pain scores of patients in the laser group in all studied time points were less than their counterparts in the placebo group for both spontaneous and chewing pain. However, no statistically significant difference were detected between the two groups except after 72 h for chewing pain with a mean pain score for the laser group [(18.84 ± 13.44) mm] less than that for the placebo group [(38.15 ± 27.06) mm]	LLLT, with the suggested parameters and under the conditions of this study, is not effective in pain reduction following initial orthodontic archwire placement.
Irfan Qamruddin *et al*., 2018 [6]	Numerical rating scale (NRS)	Consecutive 12 hours intervals for 7 days.	There was a statistically significant difference between LLLT and placebo groups in pain perceived by the patients during day, night, and on chewing for all NiTi archwires except 0.016-in and 0.018-in, which demonstrated no significant difference in spontaneous pain during day and night. However, the difference in pain on chewing remained statistically significant.	Application of LLLT at 4-week intervals can reduce the pain associated with the alignment and leveling stage of orthodontic treatment.
Song Wu *et al*., 2018 [7]	0–10 numerical rating scale (NRS) score	At 0 h, 2 h, 24 h, 4 d, and 7 d after the orthodontic forces were applied.	The mean NRS pain score was 1.0 ± 1.6 in the LG and 2.1 ± 2.3 in the PG ($P < 0.001$).	A repeated application of LLLT was able to significantly reduce self-reported pain scores.
Prasad *et al*., 2019 [8]	Visual Analog Scale (VAS)	At 6 time intervals: immediately (T0), 1 hour (T1), 3 hours (T2), 24 hours (T3), 48 hours (T4), and 7 days after activation (T5).	At T1, T2, T4, and T5, the mean pain experienced by subjects was less in patients exposed to LLLT than the placebo group, but the values were not statistically significant. At T0, higher mean pain was recorded in the experimental group as compared to the placebo group, but the difference between them was not statistically significant. Intensity of pain experienced by subjects	The study concluded that a single dose of LLLT at 980 nm, 2.5 W/cm2, and 600 J was capable of relieving post activation orthodontic pain. It was most effective in relieving pain experienced 24 hours after activation.

			in the experimental group at T3 was less as compared to the placebo group and the difference was statistically significant.	
Sfondrini *et al*., 2020 [9]	Wong-Backer faces pain rating scales (WBS)	5 minutes after band application (T0), after 1 hour (T1), after 12 hours (T2), after 24 hours (T3), and after 72 hours (T4).	The control group exhibited significantly higher WBS scores than the trial group at T0, T1, and T2. No significant differences between the two groups were reported at T3 and T4.	The present study demonstrated the efficacy of PBM in decreasing pain intensity, especially in the first 12 hours after upper first molar banding.
Matys *et al*., 2019 [10]	The numeric rating scale, NRS-11, grade level 0-10	At seven time points: 1 h, 6 h, 1 day, 2 days, 3 days, 4 days, and 5 days after the orthodontic appliance placement	The statistical analysis of the NRS-11 scores revealed significantly lower pain values in the diode laser group in contrast to the control group ($p = 0.0237$).	Our study showed that the best effects in relieving pain were obtained with a laser wavelength of 635 nm.
Nicotra *et al*., 2020 [11]	NRS (Numerical Rating Scale)	Immediately after bands cementation, 6 h, 24 h, and from day 2 to day 5	Pain experienced in the TG was significantly lower compared to both control and placebo groups, while control and placebo groups showed no differences, according to Dunn's multiple comparison test	The results of the present study evidenced that LLLT reduces the intensity of pain reported by patients after the placement of orthodontic bands
Brito *et al*., 2022 [12]	visual analog scale (VAS)	06, 24, 48, and 72 hours after the orthodontic appliance installation.	Patients that received laser therapy reported significantly lower levels of pain at 6, 24, and 48 hours than patients from the control group. At the 72-hour evaluation, the pain level was almost absent and similar between the groups.	Low-level laser therapy showed to be effective in reducing pain severity in the early stages of orthodontic treatment.

3.2. Risk of Bias of Included Studies

Given the inherent characteristics of these studies, achieving blinding of both patients and operators was nearly impractical, as the laser and the simulation (placebo) are typically administered in the same session. Consequently, the absence of single or double blinding was not deemed to significantly affect the assessment of the risk of bias in all the studies.

The risk of bias of the included RCTs is shown in Fig. 2.

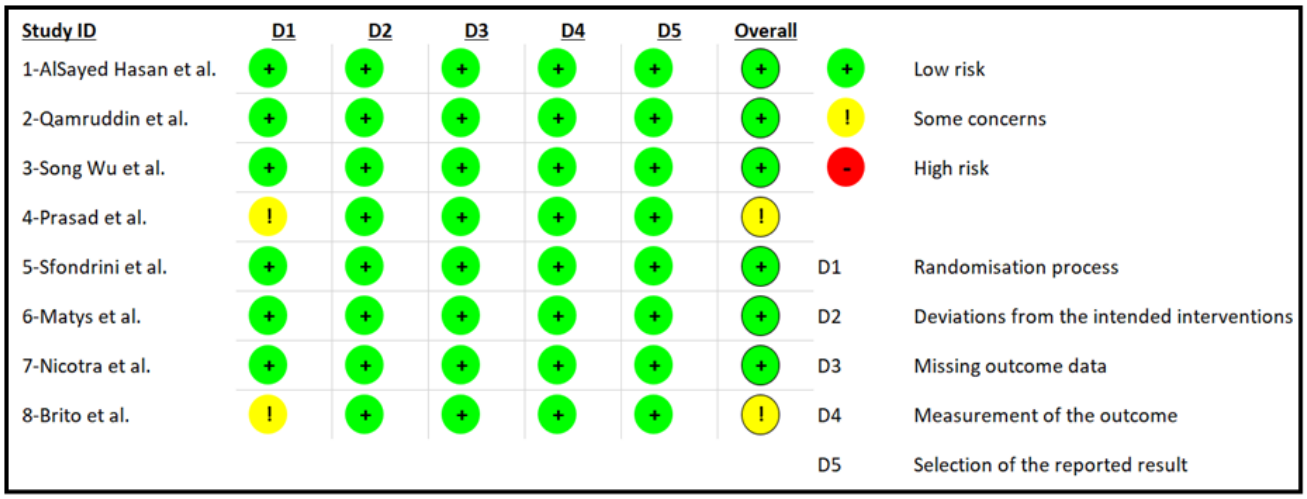

Figure 2: Risk-of-bias graph of the studies exploring pain management

Out of the total eight RCTs, two trials by Prasad *et al.,* and Brito *et al*., were assessed as having "some concerns" in the risk of biais, the rest were defined as having a low risk of biais.

Despite the exclusive inclusion of randomized studies, it was noted that the trials conducted by Prasad *et al*., and Brito *et al*., did not provide explicit descriptions of how the randomization sequence was generated.

None of the studies included in the analysis reported "incomplete outcome data" resulting from the withdrawal of a substantial number of participants.

3.3. Quality of Evidence Summary

In our systematic review, we investigated one main outcomes which is pain intensity reduction. A crucial aspect of our analysis involved assigning a quality rating to the body of evidence for the outcome across the included studies. To accomplish this, we employed the GRADE approach, a systematic method for evaluating the quality of evidence.

The GRADE approach initiates the assessment by considering the study design, distinguishing between trials and observational studies. Subsequently, it delves into five potential factors that might warrant a downgrade in the quality of evidence. These factors include the risk of bias, inconsistency, indirectness, imprecision, and publication bias.

While all the studies encompassed in our analysis adhered to the randomized controlled trial design, methodological concerns emerged that restricted the overall quality of evidence pertaining to the outcome.

The quality of evidence underwent a downgrade primarily attributed to the risk of bias assessment. This evaluation revealed that 25% of the studies were identified as having "some concerns" regarding bias associated with the randomization process. This factor introduced a level of uncertainty and potential skewing of results, influencing our confidence in the overall quality of evidence for this outcome.

Consequently, our final assessment categorized our outcome as presenting a moderate quality of evidence as detailed in Table V.

The findings from our research are carefully compiled and displayed in a detailed Summary of Findings table (table VI), utilizing the software Garde Pro GDT. This table is designed to be a central element, capturing the core essence of our research efforts with accuracy and clarity.

Table V: Quality of evidence assessement

Certainty assessment							**Certainty**
No of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	
Pain intensity							
8	Randomised trials	Not serious	Not serious	Not serious	Not serious	None	⊕⊕⊕⊕ High

Table VI: Summary of Findings table

Photobiomodulation compared to non-photobiomodulation for fixed orthodontic treatment		
Patient or population: fixed orthodontic treatment		
Setting:		
Intervention: photobiomodulation		
Comparison: non-photobiomodulation		
Outcome **№ of participants (studies)**	**Impact**	**Certainty**
pain intensity **№ of participants: 340 (8 RCTs)**	**pain reduction in orthodontic patients in at least one of the studied time points, was reported in 87.5% of the included studies (7 studies) when LLLT was applied.**	**⊕⊕⊕⊕ High**
GRADE Working Group grades of evidence High certainty: we are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.		

4. DISCUSSION

Pain is a subjective and emotionally unpleasant sensory experience linked to actual or potential tissue damage [13]. It represents one of the most common complications in orthodontics, posing a risk to patient compliance and potential withdrawal from treatment [14]. The perception of pain is highly individualized, influenced by factors such as age, gender, psychological

state, and cultural considerations [15]. Orthodontic procedures, including the placement of separating elastics, insertion and activation of arch-wires, bracket removal, and the impact of orthodontic forces, can be closely associated with the experience of pain.

The forces applied in orthodontics induce the displacement of teeth within the periodontal ligament space, resulting in bone remodeling of the alveolus through processes of resorption and apposition [16]. This tooth movement initiates an inflammatory response within the alveolar process, contributing to the experience of pain. The inflammation is attributed, in part, to the establishment of tension and compression zones within the periodontal ligament, triggering an inflammatory response characterized by the release of chemical mediators associated with hyperalgesia [15].

The early effects of orthodontic tooth movement manifest in both physical and biological alterations, impacting the extracellular matrix and various cells within the alveolar bone and periodontal ligament, including granulocytes, fibroblasts, osteoclasts, and osteoblasts. These processes commonly give rise to pain [17], as they are associated with reactions such as alterations in blood flow, the release of inflammatory cytokines (histamine, prostaglandins, encephalin, substance P, leukotrienes, etc.), stimulation of afferent A delta and C nerve fibers, neuropeptide release, and hyperalgesia [18, 19]. Earlier research has suggested that elevated levels of prostaglandin-E2 (PGE2) are associated with the initial intensity of pain, whereas an increase in interleukin-1 correlates with pain occurring 24 hours after the application of orthodontic force [20].

Various studies have examined different approaches to alleviate orthodontic pain. Among them, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) stand out as a prevalent and effective method for orthodontic pain management. NSAIDs operate by inhibiting the cyclooxygenase enzyme system, leading to a reduction in prostaglandin synthesis—an essential mediator of pain induction [21]. However, the use of NSAIDs has been associated with several side effects, including gastrointestinal issues, thrombocytopenia, skin rashes, renal insufficiency, hypertension, and headaches, as well as a decrease in the rate of tooth movement [22].

Interestingly, various alternatives have been explored to mitigate pain, such as vibrational devices, cognitive and music therapy, and other psychological interventions [23, 24]. Nonetheless, the practical application of these alternatives has been limited due to inconclusive results and a lack of robust evidence. LLLT, in contrast to NSAIDs, is associated with minimal side effects. In a randomized clinical trial conducted in 2016, Bayani *et al*., [25], conducted a comparative analysis of the effects of ibuprofen, low-level red laser (660 nm), low-level infrared laser (810 nm), and bite wafers in the management of orthodontic pain. The study found that low-level infrared laser (810 nm) emerged as the most effective approach for relieving pain after the initial wire installation. Importantly, this laser therapy proved non-invasive, painless, and aseptic, making it a potential alternative to ibuprofen without causing harm to orthodontic treatment mechanics.

Although further investigations are needed to elucidate the underlying mechanism, the analgesic action of PBM has been attributed to its neural effects, including inhibitory effects on nerve depolarization, especially C fibers, as well as its anti-inflammatory properties. Laser-induced pain reduction involves a mechanism where the laser induces changes in the conduction of action potentials in peripheral nerves. This is achieved by generating varicosities that decrease the speed of fast axonal flow and lower mitochondrial membrane potentials, leading to a reduced availability of ATP and ultimately causing neurotransmission failure in Aδ and C nociceptor fibers [26]. Additionally, LLLT exhibits localized anti-inflammatory effects, noticeable within less than 24 hours after irradiation, and contributes to the reduction of PGE2, tumor necrosis factor, plasminogen activator, and COX-2 expression [27]. Montesinos [28], suggests that another mechanism contributing to pain reduction is the stimulation of beta-endorphin production, a natural mediator produced by the organism that alleviates pain. Additionally, LLLT plays a role in inhibiting the release of arachidonic acid, which, in turn, acts on damaged cells to generate metabolites that interact with pain receptors [29].

The manifestation of pain symptoms varie in both intensity and duration, and are typically observed in the early hours following the application of forces. Pain typically initiates approximately two hours after the application of orthodontic force, peaks at 24 hours, and persists for approximately five days [30]. Numerous researchers have investigated the impact of LLLT on alleviating pain, both after the placement of elastomeric separators and during various phases of orthodontic treatment. Considering the distinct mechanisms of pain induction in each phase, the studies incorporated in this review focused on reducing post-adjustment pain in patients undergoing fixed orthodontic treatment, involving both conventional brackets and self-ligating brackets. This entails examining the reduction in pain following the placement of orthodontic arch wires.

Our review included eight articles evaluating the reduction of orthodontic pain through PBM, with seven adopting a split-mouth randomized controlled trial (RCT) design. Notably, the trial conducted by Mohammad Moaffak *et al*., the sole study indicating no statistically significant difference in pain scores at any examined time point between the laser group and the placebo group, employed a parallel arm RCT design. This difference in study design could potentially introduce subjective variations among participants.

Certain authors argue that employing a split-mouth design enhances pain evaluation by eliminating interindividual variations arising from factors such as sex, age, and pain perception [31]. When utilizing a split-mouth design, it is essential to ensure uniformity in the intervention sites for each patient. Fortunately, in orthodontics, where intact dentitions are more commonly available, achieving comparable sites is generally feasible [32]. However, it's crucial to acknowledge that the potential lack of uniformity between sites in participants might introduce selection bias, as interventions may be applied to sites with different baseline characteristics [32].

Among the eight studies, seven employed a wavelength falling within the range of 800 to 980 nm (NIR radiation). In contrast, the study by Matys *et al*., utilized Red light with a wavelength of 635 nm. The ability of light to penetrate tissues is directly influenced by the wavelength, with the penetration depth of red laser being less compared to infrared. However, in the case of the Matys *et al*., study, which utilized the minimum penetration depth is approximately 3 mm [33]. This depth is deemed adequate to reach the inner regions of the soft tissue, tooth apex, and bone, potentially elucidating the positive outcomes observed with the chosen laser wavelength. The efficacy of LLLT in pain reduction was demonstrated in six studies with a single application, and in one study, pain reduction occurred after five LLLT applications. In a study conducted by Almallah *et al*., [34], a comparison between a single dose and double dose revealed no significant differences in pain reduction. It is noteworthy that there is a lack of studies in the literature specifying the "optimal" number of LLLT applications; nevertheless, it can be inferred that a single dose post PBM application was found to be effective in alleviating pain.

In this review, pain reduction in orthodontic patients in at least one of the studied time points, was reported in 87.5% of the included studies (7 studies) when LLLT was applied. However, in one study (12.5%), no significant differences in pain intensity were observed between patients in the LLLT group and those without LLLT intervention. Hawkins and Abrahamse [35], emphasize that the dosage (or fluence) of LLLT can influence cellular processes, suggesting that a low or very low dose may not produce any effect, while very high doses may have negative or inhibiting effects. This variability in dosage might explain the contradictory results found in one study. In a study by AlSayed Hasan *et al*., [36], two different LLLT doses were compared (2.25 J/cm2/tooth and 9 J/cm2/tooth), and neither protocol demonstrated efficacy in reducing pain after the placement of elastomeric separators. Similarly, Lim *et al*., [37], compared three different protocols with application times of 15 s, 30 s, and 60 s per tooth, and none of these protocols successfully alleviated orthodontic pain resulting from the placement of elastomeric separators. The conflicting scientific evidence might be attributed to the diverse methods employed for laser irradiation, as there is currently no established protocol specifying the most effective irradiation doses. To address this, there is a pressing need for new studies with low bias risk that can ascertain the laser irradiation protocol that delivers the most potent analgesic effects in orthodontic patients.

5. CONCLUSION

We share the perspective endorsing the potential incorporation of the Low-Level Light Therapy (LLLT) protocol into routine orthodontic practice. Future investigations should strive to develop a comprehensive protocol that is both easily applicable and feasible in clinical settings. The objective is to establish a standardized approach, ensuring the secure application of laser irradiation with precisely dosed effectiveness, ultimately evolving into a recognized and routine treatment for managing orthodontic pain.

BIBLIOGRAPHY

1. Skidmore, K. J., Brook, K. J., Thomson, W. M., & Harding, W. J. (2006). Factors influencing treatment time in orthodontic patients. *American Journal of Orthodontics and Dentofacial Orthopedics*, *129*(2), 230-238.
2. Shaw, W. C. (1981). Factors influencing the desire for orthodontic treatment. *The European Journal of Orthodontics*, *3*(3), 151-162.
3. Tuby, H., Maltz, L., & Oron, U. (2007). Low-level laser irradiation (LLLI) promotes proliferation of mesenchymal and cardiac stem cells in culture. *Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery*, *39*(4), 373-378.
4. Langendam, M. W., Akl, E. A., Dahm, P., Glasziou, P., Guyatt, G., & Schünemann, H. J. (2013). Assessing and presenting summaries of evidence in Cochrane Reviews. *Systematic reviews*, *2*, 1-9.
5. AlSayed Hasan, M. M. A., Sultan, K., Ajaj, M., Voborná, I., & Hamadah, O. (2020). Low-level laser therapy effectiveness in reducing initial orthodontic archwire placement pain in premolars extraction cases: a single-blind, placebo-controlled, randomized clinical trial. *BMC Oral Health*, *20*, 1-9.
6. Qamruddin, I., Alam, M. K., Abdullah, H., Kamran, M. A., Jawaid, N., & Mahroof, V. (2018). Effects of single-dose, low-level laser therapy on pain associated with the initial stage of fixed orthodontic treatment: a randomized clinical trial. *The Korean Journal of Orthodontics*, *48*(2), 90-97.
7. Wu, S., Chen, Y., Zhang, J., Chen, W., Shao, S., Shen, H., ... & Wang, K. (2018). Effect of low-level laser therapy on tooth-related pain and somatosensory function evoked by orthodontic treatment. *International journal of oral science*, *10*(3), 22.
8. Prasad, S. M. V., Prasanna, T. R., Kumaran, V., Venkatachalam, N., Ramees, M., & Abraham, E. A. (2019). Low-level laser therapy: A noninvasive

method of relieving postactivation orthodontic pain—A randomized controlled clinical trial. *Journal of Pharmacy and Bioallied Sciences*, *11*(Suppl 2), S228-S231.
9. Sfondrini, M. F., Vitale, M., Pinheiro, A. L. B., Gandini, P., Sorrentino, L., Iarussi, U. M., & Scribante, A. (2020). Photobiomodulation and pain reduction in patients requiring orthodontic band application: randomized clinical trial. *BioMed research international*, *2020*(1), 7460938.
10. Matys, J., Jaszczak, E., Flieger, R., Kostrzewska-Kaminiarz, K., Grzech-Leśniak, K., & Dominiak, M. (2020). Effect of ozone and diode laser (635 nm) in reducing orthodontic pain in the maxillary arch—a randomized clinical controlled trial. *Lasers in medical science*, *35*, 487-496.
11. Nicotra, C., Polizzi, A., Zappalà, G., Leonida, A., Indelicato, F., & Caccianiga, G. (2020). A comparative assessment of pain caused by the placement of banded orthodontic appliances with and without low-level laser therapy: A randomized controlled prospective study. *Dentistry journal*, *8*(1), 24.
12. Brito, M. H., Nogueira, C. Q., Cotrin, P., Fialho, T., Oliveira, R. C., Oliveira, R. G., ... & Cançado, R. H. (2022). Efficacy of Low-Level Laser Therapy in Reducing Pain in the Initial Stages of Orthodontic Treatment. *International Journal of Dentistry*, *2022*(1), 3934900.
13. Merskey, H. (2007). The taxonomy of pain. *Med Clin North Am*, *91*(1), 13-20.
14. Krishnan, V. (2007). Orthodontic pain: from causes to management--a review. *Eur J Orthod*, *29*(2), 170-9.
15. Krishnan, V. (2007). Orthodontic pain: from causes to management a review. *Eur J Orthod*, *29*, 170-9.
16. Krishnan, V., & Davidovitch, Z. E. (2006). Cellular, molecular, and tissue-level reactions to orthodontic force. *American Journal of Orthodontics and Dentofacial Orthopedics*, *129*(4), 469-e1.
17. Krishnan, V. (2007). Orthodontic pain: from causes to management—a review. *The European Journal of Orthodontics*, *29*(2), 170-179.
18. Farzanegan, F., Zebarjad, S. M., Alizadeh, S., & Ahrari, F. (2012). Pain reduction after initial archwire placement in orthodontic patients: a randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics*, *141*(2), 169-173.
19. Nóbrega, C., da Silva, E. M. K., & de Macedo, C. R. (2013). Low-level laser therapy for treatment of pain associated with orthodontic elastomeric separator placement: a placebo-controlled randomized double-blind clinical trial. *Photomedicine and laser surgery*, *31*(1), 10-16.
20. Giannopoulou, C., Dudic, A., & Kiliaridis, S. (2006). Pain discomfort and crevicular fluid changes induced by orthodontic elastic separators in children. *The Journal of Pain*, *7*(5), 367-376.
21. Polat, O., & Karaman, A. I. (2005). Pain control during fixed orthodontic appliance therapy. *The Angle Orthodontist*, *75*(2), 214-219.
22. Walker, J. B., & Buring, S. M. (2001). NSAID impairment of orthodontic tooth movement. *Annals of Pharmacotherapy*, *35*(1), 113-115.
23. Lobre, W. D., Callegari, B. J., Gardner, G., Marsh, C. M., Bush, A. C., & Dunn, W. J. (2016). Pain control in orthodontics using a micropulse vibration device: A randomized clinical trial. *The Angle Orthodontist*, *86*(4), 625-630.
24. Zheng, Q., Zhang, L. H., Huang, L., Wang, G. P., Yuan, X. P., & Xu, X. M. (2016). Effects of different psychological interventions on relieving orthodontic pain in patients with different personalities: a preliminary study. *Shanghai kou Qiang yi xue= Shanghai Journal of Stomatology*, *25*(1), 91-96.
25. Bayani, S., Rostami, S., Ahrari, F., & Saeedipouya, I. (2016). A randomized clinical trial comparing the efficacy of bite wafer and low level laser therapy in reducing pain following initial arch wire placement. *Laser therapy*, *25*(2), 121-129.
26. Chow, R. T., David, M. A., & Armati, P. J. (2007). 830 nm laser irradiation induces varicosity formation, reduces mitochondrial membrane potential and blocks fast axonal flow in small and medium diameter rat dorsal root ganglion neurons: implications for the analgesic effects of 830 nm laser. *Journal of the Peripheral Nervous System*, *12*(1), 28-39.
27. Bjordal, J. M., Johnson, M. I., Iversen, V., Aimbire, F., & Lopes-Martins, R. A. B. (2006). Low-level laser therapy in acute pain: a systematic review of possible mechanisms of action and clinical effects in randomized placebo-controlled trials. *Photomedicine and Laser Therapy*, *24*(2), 158-168.
28. Montesinos, M. (1988). Experimental effects of low power laser in encephalin and endorphin synthesis. *J Eur Med Laser Assoc*, *1*(3), 2-6.
29. Shimizu, N., Yamaguchi, M., Goseki, T., Shibata, Y., Takiguchi, H., Iwasawa, T., & Abiko, Y. (1995). Inhibition of prostaglandin E2 and interleukin 1-β production by low-power laser irradiation in stretched human periodontal ligament cells. *Journal of Dental Research*, *74*(7), 1382-1388.
30. Polat, O., & Karaman, A. I. (2005). Pain control during fixed orthodontic appliance therapy. *The Angle Orthodontist*, *75*(2), 214-219.
31. Qamruddin, I., Alam, M. K., Fida, M., & Khan, A. G. (2016). Effect of a single dose of low-level laser therapy on spontaneous and chewing pain caused by elastomeric separators. *American Journal of Orthodontics and Dentofacial Orthopedics*, *149*(1), 62-66.
32. Pandis, N., Walsh, T., Polychronopoulou, A., Katsaros, C., & Eliades, T. (2013). Split-mouth designs in orthodontics: an overview with applications to orthodontic clinical trials. *European Journal of Orthodontics*, *35*(6), 783-789.
33. Nóbrega, C., da Silva, E. M. K., & de Macedo, C. R. (2013). Low-level laser therapy for treatment of pain associated with orthodontic elastomeric separator

placement: a placebo-controlled randomized double-blind clinical trial. *Photomedicine and laser surgery*, *31*(1), 10-16.

34. Almallah, M. M. E., Hajeer, M. Y., Almahdi, W. H., Burhan, A. S., Latifeh, Y., & Madkhaneh, S. K. (2020). Assessment of a single versus double application of low-level laser therapy in pain reduction following orthodontic elastomeric separation: a randomized controlled trial. *Dental and Medical Problems*, *57*(1), 45-52.
35. AlSayed Hasan, M. M. A., Sultan, K., & Hamadah, O. (2018). Evaluating low-level laser therapy effect on reducing orthodontic pain using two laser energy values: a split-mouth randomized placebo-controlled trial. *European journal of orthodontics*, *40*(1), 23-28.
36. Hawkins, D. H., & Abrahamse, H. (2006). The role of laser fluence in cell viability, proliferation, and membrane integrity of wounded human skin fibroblasts following helium-neon laser irradiation. *Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery*, *38*(1), 74-83.
37. Lim, H. M., Lew, K. K., & Tay, D. K. (1995). A clinical investigation of the efficacy of low level laser therapy in reducing orthodontic postadjustment pain. *American Journal of Orthodontics and Dentofacial Orthopedics*, *108*(6), 614-622.

