Efficacy of Laser Photobiomodulation in reducing pain induced by orthodontic tooth movement: A Systematic Review

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Abstract

Objective: To systematically review the efficacy of laser photobiomodulation in reduction of pain induced during orthodontic treatment in human participants.

Method: An extensive electronic search for randomized controlled trials and clinical controlled trials through Medline (PubMed), The Cochrane Controlled Clinical Trials Register and Science Direct till 30/12/2020 was done. Hand searching was performed for relevant journals. Reference articles were retrieved and exported to Mendeley Desktop 1.13.3 software. Risk of bias of included studies was assessed using the Cochrane risk of bias assessment tool. Articles were further analyzed using Revman 5.3 software. Forty-one articles were selected for review out of 175 retrieved articles.

Results: Around 85% of the articles indicated laser photobiomodulation to be an effective modality in reduction of pain induced during orthodontic treatment**.** Risk of bias assessment revealed 6 articles with high risk of bias, 33 articles with unclear risk and 2 with low risk.

Conclusion: Laser photobiomodulation can be a promising modality in reducing pain induced during orthodontic treatment.
Key words: Laser, photobiomodulation, Low-level laser therapy, Orthodontic pain, Systematic review.

Introduction

One of the major drawbacks and concerns of patients who undergo orthodontic treatment is the pain and discomfort during the treatment period. Patients undergoing orthodontic treatment experience pain at various stages of treatment like placement of separators, arch wire placements and activations and debonding.[1]Orthodontic tooth movement results by the continuous application of mechanical force that exceeds the elastic limit of the supporting structures of the tooth. These forces act as a physical stimulus which creates an inflammatory reaction leading to remodeling of the supporting tissues. Pain induced due to orthodontic forces shows an initial and delayed response.[1]The initial response is due to the compression of the periodontal ligament fibers and the delayed response is due to the hyperalgesia of periodontal ligaments fibers to inflammatory mediators such as bradykinin, histamine, serotonin and substance P released due to the action of prostaglandins released as the first inflammatory messengers.[2]Pain induced during orthodontic force application is due to the action of both neuropeptides and inflammatory mediators.[2]The intensity of pain produced is directly proportional to the amount of force applied. Orthodontic discomfort normally begins several hours after orthodontic force is applied, peaks after 18–36 hours, and then steadily fades after 7 days.[3] Prevention and management of pain is very important to reduce patient discomfort and improve patient compliance to treatment. Commonly used therapies for analgesia include chewing gum or hard or soft bite wavers, behavioral cognitive therapy , medications like Ibuprofen, topical application of anesthetic gel ,application of vibrational forces and nonsteroidal anti-inflammatory analgesics(NSAIDs).[3] NSAIDs are known to reduce prostaglandin synthesis, which is linked to a slower rate of tooth movement.[3]Recently photobiomodulation with lasers has been used in the field of orthodontics to reduce pain induced during orthodontic tooth movement, for accelerating tooth movement and debonding of orthodontic brackets.[4,5]Photobiomodulation has been linked to wound healing, tissue repair, relieving inflammation and edema, analgesia and for the treatment of other neurological problems.[4,5]Therapeutic window for photobiomodulation therapy lies between 1-500 mW and fluencies 1- 10 J/ cm^2.[4]The analgesic effect of photobiomodulation is linked to its photobiomodulatory effect on inflammatory process , conduction of impulses at peripheral nerve fiber endings and release of endogenous endorphins .[4,5,6] Few systematic reviews have highlighted the beneficial effects of photobiomodulation in reducing pain induced by orthodontic tooth movement.[4,5,6]However ,these reviews suggested high risk of bias, poor evidence and inconsistent results of included studies. Hence, a systematic review was planned to evaluate the efficacy of laser photobiomodulation in reducing pain induced during orthodontic treatment.

Methodology

The systematic review was conducted in accordance to the Cochrane Handbook for Systematic Reviews of Interventions following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA). [7,8]

Research question

Does Laser Photobiomodulation reduce pain induced by orthodontic tooth movement in human subjects? The research query was based on the Population, Intervention, Control, Study design (PICOS) format. (Table 1)

Search strategy for article identification

An extensive electronic search for randomized controlled trials and clinical controlled trials via three databases namely Medline (via PubMed), The Cochrane Controlled Clinical Trials Register and Science Direct was made till 31/12/2020 .Outcome of the search, Medical subjects headings (MeSH) have been summarized.(Table 2). Hand searching was performed for relevant journals. MeSH terms used in the search included "orthodontic pain", "low level / low intensity laser therapy". Boolean operators (OR, AND) were used in between the MeSH terms. Reference articles were retrieved and exported to the Mendeley Desktop 1.13.3 software.[9] Duplicate records were removed by the software. There were no language restrictions in the search. Filtered articles were then scanned by title and abstract by four reviewers to disclude articles not fitting the PICOS format. Thus, animal trials and study designs other than included criteria were discarded at this stage. The authors were not blinded to country or journal names.

Selection of studies for review:

Inclusion criteria

1. Randomized controlled trials or Clinical controlled trials evaluating the efficacy of low level laser therapy of any wavelength in pulsed or continuous mode on orthodontic pain control.
2. In -vivo studies including human research participants.
3. The studies which evaluated the outcome variables like prevalence, time course and intensity of pain assessed by means of a visual analogue scale (VAS), Numerical Rating scale and/or questionnaires.
4. Full text articles

Exclusion Criteria

1. Study designs like case reports, review articles, letters to editors, editorials etc.
2. Animal studies
3. Trials involving the use of pre-emptive analgesia or pain relief following orthognathic (jaw) surgery or dental extractions in combination with orthodontic treatment

Data extraction

Three authors searched the studies and screened the titles and abstracts of each study based on the selection criteria. Three authors independently rechecked the full-text of the screened studies. Data collected for every study included information pertaining to year of publication, authorship, geographical area, sample size, study design, control group, blinding, type of orthodontic treatment, laser parameters such as type of laser, energy density, wavelength, mode of operation, frequency and outcome.

Risk of bias assessment of included studies

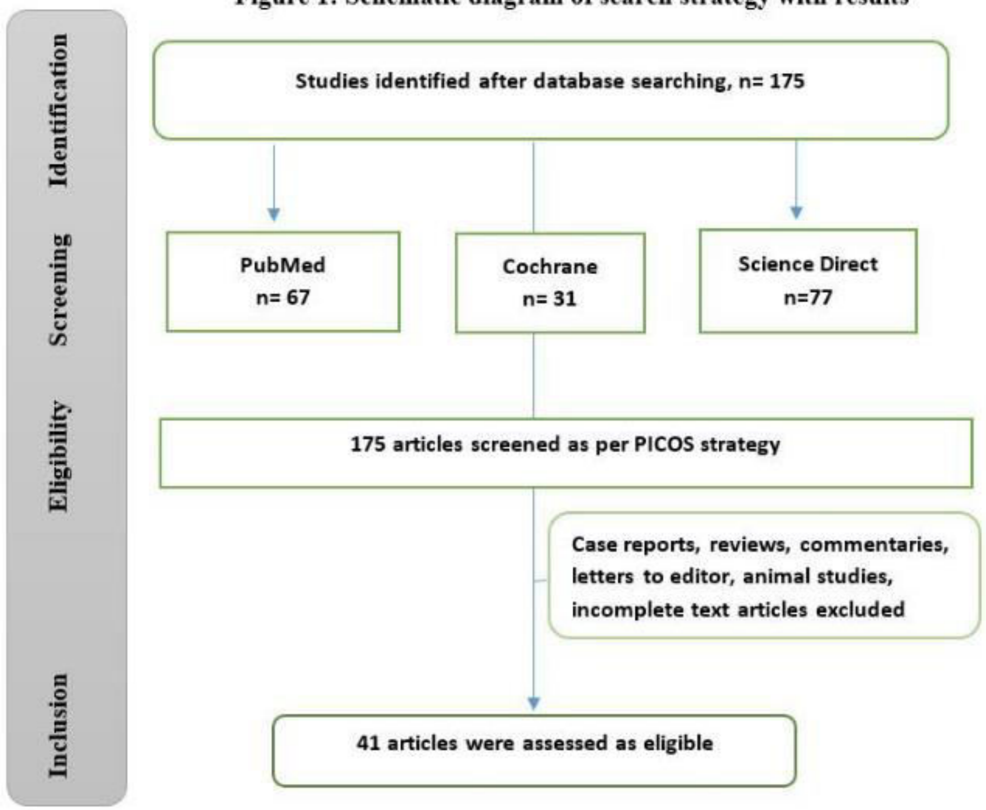
Studies were assessed for risk of bias by using the Cochrane risk of bias assessment tool.[10]Domains assessed for each included study were: sequence generation; allocation concealment; blinding of outcome assessment; completeness of outcome data; risk of selective outcome reporting; risk of other potential sources of bias. A description of the risk of bias domains was tabulated for each included trial, along with a judgement of low, high or unclear risk of bias, using the Revman 5.3 review manager software.[11] Risk of bias summary was expressed in red, green and yellow colors which referred to high, low and unclear risk of bias respectively.

Results

Search results

A total of 175 studies were retrieved through online database and hand search. After selection according to the inclusion and exclusion criteria, 41 articles were selected for the review analysis. (Figure 1)

Figure 1: Schematic diagram of search strategy with results



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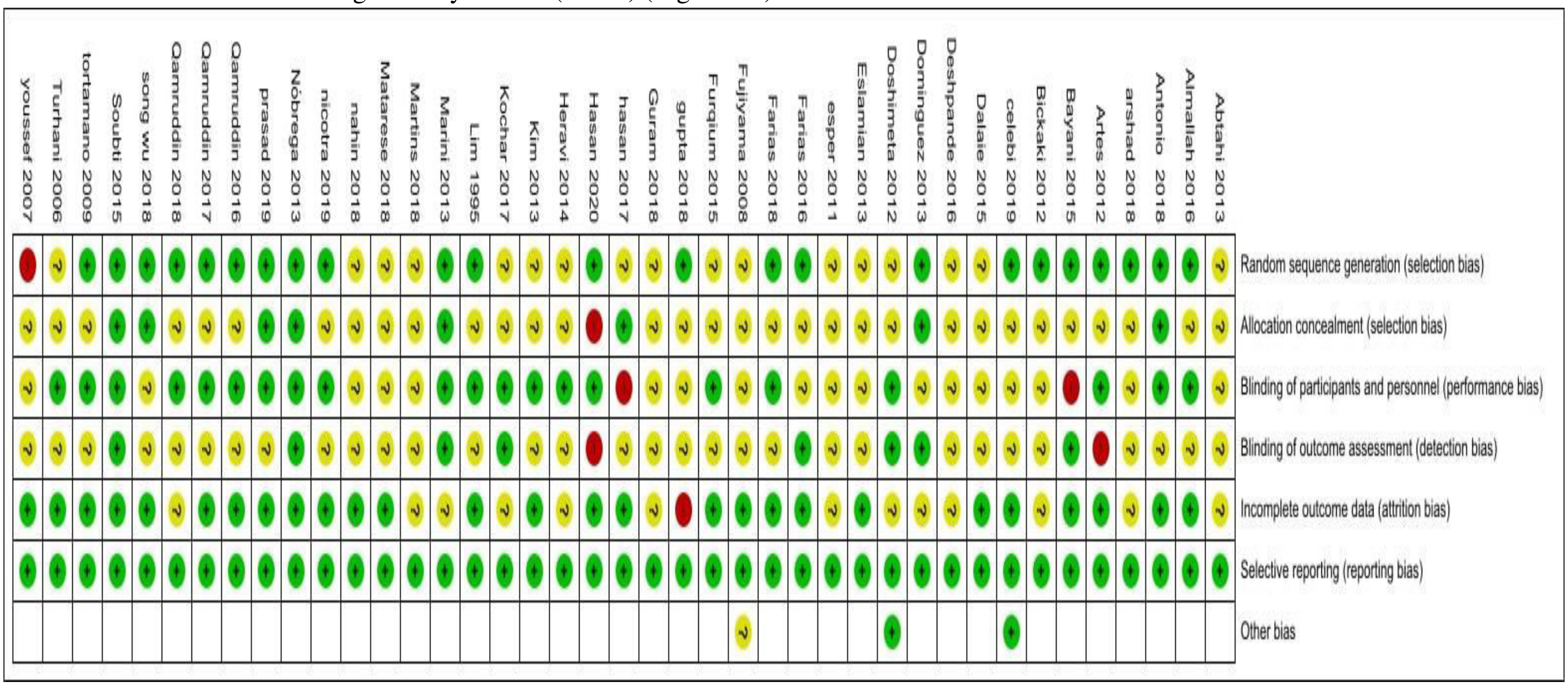
Description of included studies:

Review included 41 articles,[3,12-51]out of which 38 were randomized controlled trials and 3 were clinical controlled trials. Randomized trial designs were either split mouth or concurrent parallel. Majority of the studies used Visual Analogue Scale (VAS) to assess the pain, while few studies used questionnaire and Numerical Rating Scale (NRS).All the included studies declared that patients had signed the necessary consent forms. The characteristics and laser parameters of the included studies are enumerated in the tables 3 and 4.

Assessment of risk of bias:

Risk of bias assessment revealed, 6 articles with high risk of bias, 33 articles with unclear risk and 2 with low risk. (Figure 2A). Majority of studies reported bias involved in their studies. However, information about concealed randomization and blinding of outcome assessment was missing in many studies (>75%).(Figure 2B).



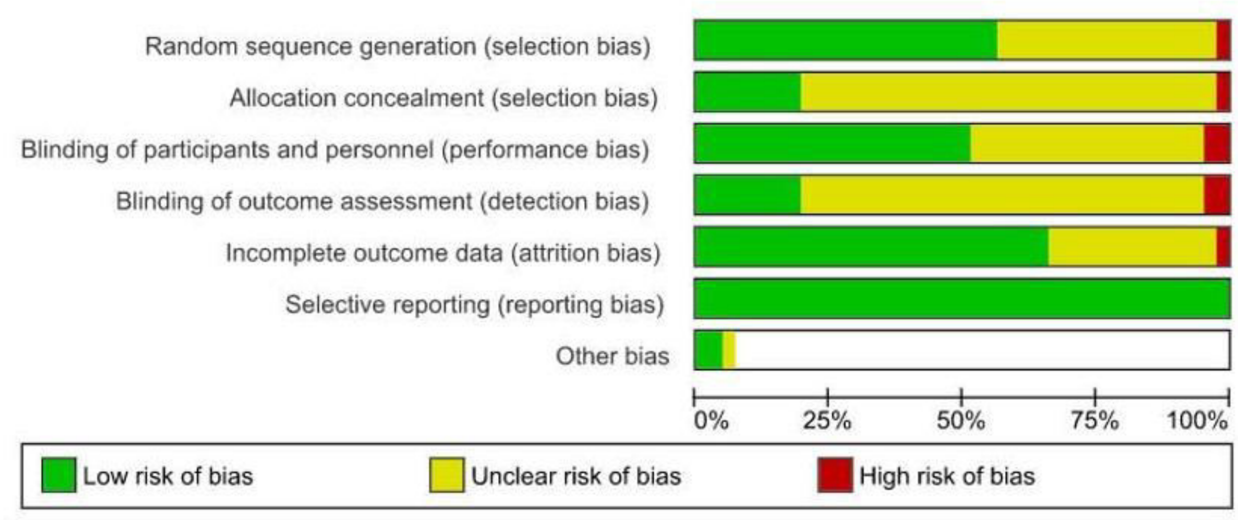


Figure 2B:Risk of Bias summary

Discussion

Orthodontic pain is the most common reason which prevents patients from undergoing fixed mechano-therapy. Non-steroidal anti-inflammatory drugs (NSAIDs) used to relieve pain are associated with side effects like allergy, gastric ulceration, bleeding disorders, skin rashes, hypertension and most importantly they inhibit the prostaglandin synthesis thereby affecting the rate of orthodontic teeth movement.[52]Laser photobiomodulation therapy is a non-invasive, non- pharmacological method of alleviating orthodontic pain. According to few studies, pain treatment with low-level lasers (810 nm) was more effective than analgesics.[28.34,39,40] Laser photobiomodulation reduces levels of PGE2 (prostaglandin E2), tumor necrosis factor, plasminogen activator, and COX-2 (cyclooxygenase) expression and enhances local effects of inflammation in less than 24 hours after irradiation.[53] One of the mechanisms by which laser irradiation reduces pain is by altering the conduction of action potentials in peripheral nerves by generating varicosities that slow down fast axonal flow and lower mitochondrial membrane potentials, resulting in decreased adenosine-tri-phosphate (ATP) availability and neurotransmission failure in A and C nociceptor fibres.[54] Low level laser therapy stimulates production of beta-endorphin, a natural pain-relieving mediator produced by the body and reduces the release of arachidonic acid, a metabolite that interacts with pain receptors when it acts on injured cells.[55]Clinical results of low level laser therapy depend on the dosimetry such as wavelength, energy density (J/cm^2), time, and frequency. GaAs-Al (Gallium Arsenide Aluminum)diode laser was more widely used than other types in the studies included in the review as they have a superior tissue penetration property compared to other lasers and is known to produce advanced analgesic effect.[13] Twenty five studies which showed effective analgesia with laser photobiomodulation used 809–940 nm GaAs-Al laser and four studies used 632.8–670 nm (Helium-Neon[He-Ne] , Aluminum Gallium Indium Phosphide [InGaAlP]).[13,26,28-29]These favorable wavelengths fall into an "optical windowat red and near infrared wavelengths (600–1070 nm). Wavelengths between 810 to 840 nm (GaAsAl) are shown to have greatest analgesic activity because they exhibit effective penetration depth into alveolar bone and periodontal supporting tissues due to their low absorbance in hemoglobin and water.[27] A study conducted by Fujiyama et al used CO_2 laser (outside the range of near infra-red region) and found it effective in reducing orthodontic pain without affecting the tooth movement.[15]Esper et al and Kim et al studied the effect of non- coherent light on the orthodontic pain induced due to tooth movement.[17,26] Esper et al compared 660 nm, InGaAlP laser with 640 nm GaAlAs light emitting diode (LED) light and found a significant reduction in pain in the LED group compared to the laser group. [17]The laser parameters used in the study might have contributed to pain reduction along with high-potency and high-energy light emitting diode used. Frequency of laser application followed in most of the trials were only a single dose of irradiation within 7–14 days of follow-up. All the studies considered for review used laser irradiation in continuous wave mode. However, some studies have pointed out towards multiple photo-dissociation events occurringat pulsed mode, promoting more laser light penetration than in continuous mode, where the number of dissociations may be substantially lower. When compared to continuous wave light, certain studies have shown that pulsed light promotes better tissue regeneration and lessens the behavioral symptoms of somatic pain.[4,56] Majority of studies (21 studies) demonstrated pain reduction after a single laser application, while pain was reduced after two applications in three studies [15, 22, 32],and more than two applications in eleven studies. Almallah et al, conducted a study comparing single dose to double dose of laser irradiation and found no significant difference in pain reduction between the groups.[32]We found no research in the literature that reported the "optimal" number of LLLT treatments for analgesia; nonetheless, based on the findings of the review it can be purported that single dose of laser irradiation was enough to alleviate pain.

Assessment of pain is one of the most challenging factors, as it is extremely subjective and it can vary according to individual characteristics such as age, gender, pain threshold of the individual, emotional state, stress and type of orthodontic treatment. The magnitude of the force applied on each patient and during each treatment stage vary which makes it difficult to measure and quantify pain. Reduction in pain with photobiomodulation was observed during arch wire placement, [13,16,21,28,35,46-48] canine retraaction,[20,34,45,51] ,elastomeric separation, [12,15,24-26,32-33,36,38-44] and molar banding.[19]Using split mouth technique reduces inter individual heterogeneity due to sex, age, pain perception and type of treatment. Also split mouth technique requires small sample size and balances dropout between groups.[4]Majority of studies in the review used split mouth design. Measuring the pain threshold and the changes in pain intensity is challenging because of its extremely subjective nature. VAS is considered as the most dependable method to analyze the change of pain not only in orthodontic cases but in many clinical scenarios.[4] Most of the studies (30 studies) reviewed, used VAS as a method to evaluate the intensity of pain. Qamruddin et al in all their three studies used numerical rating scale and concluded it to be a convenient approach for collecting information over telephone conversations. [25,27,36] Tortamano et al used a questionnaire method with added numeric rating scale to analyze the pain and considered it as a drawback of the study.[57]

Pain due to orthodontic treatment is known to start by 4th hour of application, increases to its peak by 24th hour and disappears by 4-7 days.[46] Majority of the studies concluded that the maximum intensity of pain was recorded at second day .Song Vu et al, concluded that LLLT treatment affected not only the treatment side but also the non-treatment side, indicating that there is a generalized analgesic effect mediated by photobiomodulation through trigeminal system.[45]Turhani et al summarized that laser application reduced the pain prevalence at 6 and 30 hours after intervention .[13]

Bjordal et al. [10] observed beneficial effects of LLLT on acute pain by using a dose of 7.5 J/cm2 for the first 72 hours after the injury to reduce inflammation; gradually tapering to 2 J/cm2 to encourage tissue repair.[53]Majority of the studies in the present review observed effective pain inhibition at doses between 5 and 20 J/cm2 for severe pain. Some authors claim that larger dosages are required to alleviate orthodontic pain, such as 35 J/cm^2 and that doses of 5 J/cm^2 and less were ineffective.[4,58] Both Qamruddin et al,[36]and Artés-Ribas et al,[18]reported successful therapy using the same total energy (12 J/cm2per tooth) but different wavelengths, 940 nm and 830 nm, respectively. Artés-Ribas et al.[18] and Bicakci et al. [19]who were likewise successful in lowering orthodontic pain, employed wavelengths and dosages (6J/cm2/tooth) that were similar; however, their total energies were different, at 12J/cm2 and 1J/cm2, respectively. The laser irradiation parameters must be chosen depending on the clinical scenario, taking into account the optical properties of the tissue to be irradiated, and the laser irradiation methods (point or sweep, contact or noncontact). The dose administered to the tissue can be varied by modifying the spot size. By reducing the spot size, the energy density supplied to the tissue can be increased, resulting in higher irradiance and laser penetration into biological tissue. Majority of the studies reported either incomplete or ambiguous laser parameters, missing critical details including spot size, energy density per spot and per tooth, application time/spot, and total energy per spot and per tooth. Inconsistency in reporting laser parameters makes it difficult for researchers to compare results across studies and establish clinical practice guidelines. Hence, it is recommended to follow and report laser parameters used in the studies based on WALT (World Association for Laser Therapy) guidelines.[59]

Conclusion

Majority of studies included in the review, demonstrated beneficial effect of laser photobiomodulation in reducing pain induced by orthodontic treatment like arch wire activation, elastomeric teeth separation, canine retraction and molar banding. Being cognizant about heterogeneity in reporting of laser parameters and high prevalence of risk of bias in the studies included in this review, the evidence should be considered with caution.

References

1. Krishnan V. Orthodontic pain: from causes to management--a review. Eur J Orthod. 2007 Apr;29(2):170-9. doi: 10.1093/ejo/cjl081.
2. Erdinç AM, Dinçer B. Perception of pain during orthodontic treatment with fixed appliances. Eur J Orthod. 2004 Feb;26(1):79-85. doi: 10.1093/ejo/26.1.79.
3. AlSayed Hasan MMA, Sultan K, Ajaj M, Voborná I, Hamadah O. 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. 2020 Jul 20;20(1):209. doi: 10.1186/s12903-020-01191-7.
4. Deana NF, Zaror C, Sandoval P, Alves N. Effectiveness of Low-Level Laser Therapy in Reducing Orthodontic Pain: A Systematic Review and Meta-Analysis. Pain Res Manag. 2017;2017:8560652. doi: 10.1155/2017/8560652. Epub 2017 Sep 27.
5. Sonesson, M., De Geer, E., Subraian, J. *et al.* Efficacy of low-level laser therapy in accelerating tooth movement, preventing relapse and managing acute pain during orthodontic treatment in humans: a systematic review. *BMC Oral Health* **17,** 11 (2017). https://doi.org/10.1186/s12903-016-0242-8
6. Li FJ, Zhang JY, Zeng XT, Guo Y. Low-level laser therapy for orthodontic pain: a systematic review. Lasers Med Sci. 2015 Aug;30(6):1789-803. doi: 10.1007/s10103-014-1661-x. Epub 2014 Sep 26.
7. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org.
8. *Moher D*, *Liberati* A, *Tetzlaff J*, *Altman DG*, *Group* P. *Preferred reporting items* for *systematic reviews* and *meta-analyses*: the *PRISMA statement*. *Int J Surg* (*2010*) 8(5):336–341. doi:10.1016/j.ijsu.2010.02.007
9. Patak AA, Naim HA, Hidayat R. Taking Mendeley as multimedia-based application in academic writing. International Journal on Advanced Science, Engineering and Information Technology. 2016 Aug;6(4):557-560.
10. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savović J, Schulz KF, Weeks L, Sterne JA. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Bmj. 2011 Oct 18;343:d5928.
11. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
12. Lim HM, Lew KK, Tay DK. A clinical investigation of the efficacy of low level laser therapy in reducing orthodontic postadjustment pain. Am J Orthod Dentofacial Orthop. 1995 Dec;108(6):614-22. doi: 10.1016/s0889-5406(95)70007-2.
13. Turhani D, Scheriau M, Kapral D, Benesch T, Jonke E, Bantleon HP. Pain relief by single low-level laser irradiation in orthodontic patients undergoing fixed appliance therapy. Am J Orthod Dentofacial Orthop. 2006 Sep;130(3):371-7. doi: 10.1016/j.ajodo.2005.04.036.

14. Youssef M, Ashkar S, Hamade E, Gutknecht N, Lampert F, Mir M. The effect of low-level laser therapy during orthodontic movement: a preliminary study. Lasers Med Sci. 2008 Jan;23(1):27-33. doi: 10.1007/s10103-007-0449-7.
15. Fujiyama K, Deguchi T, Murakami T, Fujii A, Kushima K, Takano-Yamamoto T. Clinical effect of CO(2) laser in reducing pain in orthodontics. Angle Orthod. 2008 Mar;78(2):299-303. doi: 10.2319/033007-153.1.
16. Tortamano A, Lenzi DC, Haddad AC, Bottino MC, Dominguez GC, Vigorito JW. Low-level laser therapy for pain caused by placement of the first orthodontic archwire: a randomized clinical trial. Am J Orthod Dentofacial Orthop. 2009 Nov;136(5):662-7. doi: 10.1016/j.ajodo.2008.06.028.
17. Esper MA, Nicolau RA, Arisawa EA. The effect of two phototherapy protocols on pain control in orthodontic procedure--a preliminary clinical study. Lasers Med Sci. 2011 Sep;26(5):657-63. doi: 10.1007/s10103-011-0938-6.
18. Artés-Ribas M, Arnabat-Dominguez J, Puigdollers A. Analgesic effect of a low-level laser therapy (830 nm) in early orthodontic treatment. Lasers Med Sci. 2013 Jan;28(1):335-41. doi: 10.1007/s10103-012-1135-y.
19. Bicakci AA, Kocoglu-Altan B, Toker H, Mutaf I, Sumer Z. Efficiency of low-level laser therapy in reducing pain induced by orthodontic forces. Photomed Laser Surg. 2012 Aug;30(8):460-5. doi: 10.1089/pho.2012.3245.
20. Doshi-Mehta G, Bhad-Patil WA. Efficacy of low-intensity laser therapy in reducing treatment time and orthodontic pain: a clinical investigation. Am J Orthod Dentofacial Orthop. 2012 Mar;141(3):289-297. doi: 10.1016/j.ajodo.2011.09.009.
21. Domínguez A, Velásquez SA. Effect of low-level laser therapy on pain following activation of orthodontic final archwires: a randomized controlled clinical trial. Photomed Laser Surg. 2013 Jan;31(1):36-40. doi: 10.1089/pho.2012.3360.
22. Eslamian L, Borzabadi-Farahani A, Hassanzadeh-Azhiri A, Badiee MR, Fekrazad R. The effect of 810-nm low-level laser therapy on pain caused by orthodontic elastomeric separators. Lasers Med Sci. 2014 Mar;29(2):559-64.doi: 10.1007/s10103-012-1258-1.
23. Abtahi SM, Mousavi SA, Shafaee H, Tanbakuchi B. Effect of low-level laser therapy on dental pain induced by separator force in orthodontic treatment. Dent Res J (Isfahan). 2013 Sep;10(5):647-51. PMID: 24348624; PMCID: PMC3858741.
24. Marini I, Bartolucci ML, Bortolotti F, Innocenti G, Gatto MR, Alessandri Bonetti G. The effect of diode superpulsed low-level laser therapy on experimental orthodontic pain caused by elastomeric separators: a randomized controlled clinical trial. Lasers Med Sci. 2015 Jan;30(1):35-41. doi: 10.1007/s10103-013-1345-y.
25. Nóbrega C, da Silva EM, de Macedo CR. Low-level laser therapy for treatment of pain associated with orthodontic elastomeric separator placement: a placebo-controlled randomized double-blind clinical trial. Photomed Laser Surg. 2013 Jan;31(1):10-6. doi: 10.1089/pho.2012.3338.
26. Kim WT, Bayome M, Park JB, Park JH, Baek SH, Kook YA. Effect of frequent laser irradiation on orthodontic pain. A single-blind randomized clinical trial. Angle Orthod. 2013 Jul;83(4):611-6. doi: 10.2319/082012-665.1.

27. Heravi F, Moradi A, Ahrari F. The effect of low level laser therapy on the rate of tooth movement and pain perception during canine retraction. Oral Health Dent Manag. 2014 Jun;13(2):183-8. PMID: 24984620.
28. Bayani S, Rostami S, Ahrari F, Saeedipouya I. A randomized clinical trial comparing the efficacy of bite wafer and low level laser therapy in reducing pain following initial arch wire placement. Laser Ther. 2016 Jun 29;25(2):121-129. doi: 10.5978/islsm.16-OR-10.
29. Sobouti F, Khatami M, Chiniforush N, Rakhshan V, Shariati M. Effect of single-dose low-level helium-neon laser irradiation on orthodontic pain: a split-mouth single-blind placebo-controlled randomized clinical trial. Prog Orthod. 2015;16:32. doi: 10.1186/s40510-015-0102-0.
30. Furquim RD, Pascotto RC, Rino Neto J, Cardoso JR, Ramos AL. Low-level laser therapy effects on pain perception related to the use of orthodontic elastomeric separators. Dental Press J Orthod. 2015 May-Jun;20(3):37-42. doi: 10.1590/2176-9451.20.3.037-042.oar.
31. Dalaie K, Hamedi R, Kharazifard MJ, Mahdian M, Bayat M. Effect of Low-Level Laser Therapy on Orthodontic Tooth Movement: A Clinical Investigation. J Dent (Tehran). 2015 Apr;12(4):249-56.
32. Almallah MM, Almahdi WH, Hajeer MY. Evaluation of Low Level Laser Therapy on Pain Perception Following Orthodontic Elastomeric Separation: A Randomized Controlled Trial. J Clin Diagn Res. 2016 Nov;10(11):ZC23-ZC28. doi: 10.7860/JCDR/2016/22813.8804.
33. Farias RD, Closs LQ, Miguens SA Jr. Evaluation of the use of low-level laser therapy in pain control in orthodontic patients: A randomized split-mouth clinical trial. Angle Orthod. 2016 Mar;86(2):193-8. doi: 10.2319/122214-933.1.
34. Kochar GD, Londhe SM, Varghese B, Jayan B, Kohli S, Kohli VS. Effect of low-level laser therapy on orthodontic tooth movement. Journal of Indian Orthodontic Society. 2017 Jun;51(2):81-6.doi: 10.4103/jios.jios_200_16
35. Deshpande P, Patil K, Mahima VG, Shivalinga BM, Suchetha M, Ranjan A. Low-level laser therapy for alleviation of pain from fixed orthodontic appliance therapy: a randomized controlled trial. Journal of Advanced Clinical and Research Insights. 2016 Mar 1;3(2):43-6.doi: 10.15713/ins.jcri.103
36. Qamruddin I, Alam MK, Fida M, Khan AG. Effect of a single dose of low-level laser therapy on spontaneous and chewing pain caused by elastomeric separators. Am J Orthod Dentofacial Orthop. 2016 Jan;149(1):62-6. doi: 10.1016/j.ajodo.2015.06.024.
37. AlSayed Hasan MMA, Sultan K, Hamadah O. Evaluating low-level laser therapy effect on reducing orthodontic pain using two laser energy values: a split-mouth randomized placebo-controlled trial. Eur J Orthod. 2018 Jan 23;40(1):23-28. doi: 10.1093/ejo/cjx013.

38. Qamruddin I, Alam MK, Mahroof V, Fida M, Khamis MF, Husein A. Effects of low-level laser irradiation on the rate of orthodontic tooth movement and associated pain with self-ligating brackets. Am J Orthod Dentofacial Orthop. 2017 Nov;152(5):622-630. doi: 10.1016/j.ajodo.2017.03.023.
39. Guram G, Reddy RK, Dharamsi AM, Syed Ismail PM, Mishra S, Prakashkumar MD. Evaluation of Low-Level Laser Therapy on Orthodontic Tooth Movement: A Randomized Control Study. Contemp Clin Dent. 2018 Jan-Mar;9(1):105-109. doi: 10.4103/ccd.ccd_864_17.
40. Matarese, G.; Matarese, M.; Picciolo, G.; Fiorillo, L.; Isola, G. Evaluation of Low-Level Laser Therapy with Diode Laser for the Enhancement of the Orthodontic Tooth Movement: a Split-Mouth Study. Preprints 2018, 2018090273 doi: 10.20944/preprints201809.0273.v1.
41. Arshad F, Dharmesh HS, Bharathi VS, Ram AA, Begum S. Effect of Two Energy Values of 810-nm Diode Low-Level Laser Therapy on Reducing Pain Caused by Orthodontic Elastomeric Separators: ASplit Mouth Randomized Controlled Clinical Study. Int J Prev Clin Dent Res 2018;5(2):42-45. Availablefrom :http://www.ijpcdr.com/pdf/2018/April-June/9_DR_FAISAL_DR%20DHARMESH.pdf.Acessed on 13-4-2021
42. Farias RD, Closs LQ, Miguens SA Jr. Low-level laser therapy effects on pain perception related to the use of orthodontic elastomeric separators. Dental Press J Orthod. 2015 May-Jun;20(3):37-42. doi: https://doi.org/10.2319/122214-933.1.
43. Gupta S, Ahuja S, Bhambri E, Sharma S, Sharma R, Kalia H. Evaluating the effect of low-level laser therapy on pain induced by orthodontic separation: a randomized split-mouth clinical trial. Laser Dent Sci. 2018;2(4):221-8. doi:10.1007/s41547-018-0040-5
44. Martins IP, Martins RP, Caldas SGFR, Dos Santos-Pinto A, Buschang PH, Pretel H. Low-level laser therapy (830 nm) on orthodontic pain: blinded randomized clinical trial. Lasers Med Sci. 2019 Mar;34(2):281-286. doi: 10.1007/s10103-018-2583-9.
45. Wu S, Chen Y, Zhang J, Chen W, Shao S, Shen H, Zhu L, Ye P, Svensson P, Wang K. Effect of low-level laser therapy on tooth-related pain and somatosensory function evoked by orthodontic treatment. Int J Oral Sci. 2018 Jul 2;10(3):22. doi: 10.1038/s41368-018-0023-0.
46. Nahin J, Arshad F, Srinivas BV, Kumar S, Lokesh NK. The Efficacy of Low-level Laser Therapy on Pain caused by Placement of the First Orthodontic Archwire: A Clinical Study. J Contemp Dent Pract. 2018 Apr 1;19(4):450-455. PMID: 29728552.
47. Qamruddin I, Alam MK, Abdullah H, Kamran MA, Jawaid N, Mahroof V. Effects of single-dose, low-level laser therapy on pain associated with the initial stage of fixed orthodontic treatment: A randomized clinical trial. Korean J Orthod. 2018 Mar;48(2):90-97. doi: 10.4041/kjod.2018.48.2.90.

48. Lo Giudice A, Nucera R, Perillo L, Paiusco A, Caccianiga G. Is Low-Level Laser Therapy an Effective Method to Alleviate Pain Induced by Active Orthodontic Alignment Archwire? A Randomized Clinical Trial. J Evid Based Dent Pract. 2019 Mar;19(1):71-78. doi: 10.1016/j.jebdp.2018.11.001.
49. Celebi F, Turk T, Bicakci AA. Effects of low-level laser therapy and mechanical vibration on orthodontic pain caused by initial archwire. Am J Orthod Dentofacial Orthop. 2019 Jul;156(1):87-93. doi: 10.1016/j.ajodo.2018.08.021.
50. Nicotra C, Polizzi A, Zappalà G, Leonida A, Indelicato F, Caccianiga G. 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. Dent J (Basel). 2020 Mar 4;8(1):24. doi: 10.3390/dj8010024.
51. Prasad SMV, Prasanna TR, Kumaran V, Venkatachalam N, Ramees M, Abraham EA. Low-Level Laser Therapy: A Noninvasive Method of Relieving Postactivation Orthodontic Pain-A Randomized Controlled Clinical Trial. J Pharm Bioallied Sci. 2019 May;11(Suppl 2):S228-S231. doi: 10.4103/JPBS.JPBS_303_18.
52. Xiaoting L, Yin T, Yangxi C. Interventions for pain during fixed orthodontic appliance therapy. A systematic review. Angle Orthod. 2010 Sep;80(5):925-32. doi: 10.2319/010410-10.1.
53. Bjordal JM, Johnson MI, Iversen V, Aimbire F, Lopes-Martins RA. Low-level laser therapy in acute pain: a systematic review of possible mechanisms of action and clinical effects in randomized placebo-controlled trials. Photomed Laser Surg. 2006 Apr;24(2):158-68. doi: 10.1089/pho.2006.24.158.
54. Chow R. T., David M. A., Armati P. J. 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. *2007;12(1):28–39.* doi: 10.1111/j.1529-8027.2007.00114.x.
55. Shimizu N, Yamaguchi M, Goseki T, Shibata Y, Takiguchi H, Iwasawa T, Abiko Y. Inhibition of prostaglandin E2 and interleukin 1-beta production by low-power laser irradiation in stretched human periodontal ligament cells. J Dent Res. 1995 Jul;74(7):1382-8. doi: 10.1177/00220345950740071001.
56. Hashmi JT, Huang YY, Sharma SK, Kurup DB, De Taboada L, Carroll JD, Hamblin MR. Effect of pulsing in low-level light therapy. Lasers Surg Med. 2010 Aug;42(6):450-66. doi: 10.1002/lsm.20950.
57. Tortamano A, Lenzi DC, Haddad AC, Bottino MC, Dominguez GC, Vigorito JW. Low-level laser therapy for pain caused by placement of the first orthodontic archwire: a randomized clinical trial. Am J Orthod Dentofacial Orthop. 2009 Nov;136(5):662-7. doi: 10.1016/j.ajodo.2008.06.028.
58. Angelieri F., Sousa M. V. D. S., Kanashiro L. K., Siqueira D. F., Maltagliati L. Á. Effects of low intensity laser on pain sensitivity during orthodontic movement. *Dental Press Journal of Orthodontics*. 2011;16(4):95–102. doi: 10.1590/S2176-94512011000400016.

59. Bjordal JM. Low level laser therapy (LLLT) and World Association for Laser Therapy (WALT) dosage recommendations. Photomed Laser Surg. 2012 Feb;30(2):61-2. doi: 10.1089/pho.2012.9893.

Table 1: PICOS format (Population, Intervention, Control,Outcome, Study design) formulated to identify studies pertaining to research question formulated.

Population	Human subjects undergoing fixed orthodontic treatment
Intervention	Low level laser therapy for reducing pain induced by orthodontic tooth movement
Control	Simulated (Sham) laser therapy, conventional analgesia through medications, Placebo Treatment
Outcome	Reduction in pain assessed by Visual Analogue Scale, Questionnaire, Numeric Rating Scale
Study	Randomized controlled, clinical controlled trials

Table 2: Search strategy

Data base	Search Strategy	Articles retrieved
PubMed	("low-level light therapy"[MeSH Terms] OR ("low-level"[All Fields] AND "light"[All Fields] AND "therapy"[All Fields]) OR "low-level light therapy"[All Fields] OR ("low"[All Fields] AND "level"[All Fields] AND "laser"[All Fields] AND "therapy"[All Fields]) OR "low level laser therapy"[All Fields]) AND orthodontic[All Fields] AND ("pain"[MeSH Terms] OR "pain"[All Fields])	67
Cochrane Database of Clinical Trials	“low-level laser therapy” AND “orthodontic” AND “pain”	31
Science direct	Low-level OR laser AND therapy OR low-level laser therapy AND orthodontic AND pain	77

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Table 3: Study characteristics

Sl no	Author, Year, Country	Study design	Control group	Blinding	Orthodontic Intervention	Pain Assessment
1	Lim et al, 1995, Singapore[12]	RCT	PL, SL	DB	ES	VAS
2	Turhani et al,2006 ,Austria[13]	RCT	PL, SL	SB	AWP	QM
3	Youssef et al, ,2007, Syria[14]	CCT	PL, SL	NM	SA	VAS
4	Fujiyama et al, 2008, Japan[15]	RCT	NSAIDs	SB	ES	VAS
5	Tortamano et al, 2009, Brazil[16]	RCT	PL, NSAIDs	DB	AWP	QM, NRS
6	Esper et al, 2011, Brazil[17]	CCT	PL, SL	NM	ES	VAS
7	Artes-Ribas et al,2012, Spain[18]	RCT	PL	NM	ES	VAS
8	Bicakci et al, 2012, Turkey[19]	RCT	PL	NM	MB	VAS
9	Doshi-Mehta et al, 2012, India[20]	RCT	PL, SL	DB	CR	VAS
10	Domı´nguez A et al, 2013, Colombia[21]	RCT	PL, SL	DB	AWP	VAS
11	Eslamian et al, 2013, Iran[22]	RCT	NSAIDs	NM	ES	VAS
12	Abtahi et al, 2013, Iran[23]	RCT	PL, SL	NM	ES	VAS
13	Marini et al, 2013, Italy [24]	RCT	PL, SL, NSAIDs	TB	ES	VAS
14	Nóbregaet al, 2013, Brazil [25]	RCT	PL, SL	DB	ES	VAS
15	Kim et al, 2013, Korea [26]	RCT	PL, NSAIDs	SB	ES	VAS
16	Heravi et al, 2014,Iran [27]	RCT	PL	SB	SA	VAS
17	Bayani et al,2015,Iran [28]	RCT	PL, NSAIDs, Bite wafer	SB	AWP	VAS
18	Sobouti et al ,2015 ,Iran[29]	RCT	PL, SL	SB	CR	VAS
19	Furquim et al , 2015,Brazil [30]	RCT	PL, SL,	SB	ES	VAS
20	Dalaie et al, 2015,Iran[31]	RCT	NSAIDs	DB	CR	QM
21	Almallah et al, 2016,Syria[32]	RCT	PL SL	SB	ES	VAS
22	Farias et al, 2016 ,Brazil[33]	RCT	PL SL	TB	ES	VAS
23	Kochar et al, 2016,India[34]	RCT	NSAIDs	SBS	CR	VAS
24	Deshpande et al, 2016, India [35]	RCT	SL, NSAIDs	NM	AWP	QM
25	Qamruddin et al, 2016, Malaysia[36]	RCT	PL, SL	SB	ES	NRS

26	Hasan et al. 2017,Syria[37]	RCT	PL, SL	SB	ES	VAS
27	Qamruddin et al ,2017,Pakistan[38]	RCT	PL, SL	SB	ER	NRS
28	Guram et al, 2018,India[39]	RCT	NSAIDs	DB	ER	QM
29	Matarese et al, 2018,Italy[40]	RCT	NSAIDs	NM	ER	VAS
30	Arshad et al,2018,India[41]	RCT	PL, SL	NM	ER	VAS
31	Farias et al ,2018,Brazil[42]	RCT	PL, SL	DB	ER	VAS
32	Gupta et al,2018 ,India[43]	RCT	PL, SL	NM	ER	VAS
33	Martins et al,2018,Brazil[44]	RCT	PL, SL	DB	ER	VAS
34	Song Wu et al,2018,China[45]	RCT	PL	DB	CR	NRS
35	Nahin et al, 2018, India[46]	CCT	NSAIDs	NM	AWP	VAS
36	Qamruddin et al 2018, Pakistan [47]	RCT	PL, SL	SB	AWP	NRS
37	Antonio et al 2019, Italy[48]	RCT	PL,SL	SB	AWP	NRS
38	Celebi et al, 2019, Turkey[49]	RCT	PL, Vibration	NM	AWP	VAS
39	Nicotra et al 2019, Italy[50]	RCT	PL, SL	SB	ER	NRS
40	Prasad et al 2019, India[51]	RCT	PL	SB	CR	VAS
41	Hasan et al 2020, Syria[3]	RCT	PL	SB	AWP	VAS

RCT-Randomized controlled trial, CCT-Controlled clinical trial, PL-placebo, SL-simulated laser, NSAIDs-Non steroidal anti-inflammatory analgesics-Single blinding, DB-Double Blinding,TB-Triple blinding, AWA-Arch wire activation-Canine retraction, MB-Molar Banding, ES-Elastomeric separators, VAS-Visual Analogue Scale, NRS-Numerical Rating Scale, QM-Questionnaire method

Table 4: Laser parameters and outcome of studies

Sl no	Author	Laser Wavelength Mode of delivery	Power Output	Time per site	Frequency of intervention	Energy density per point(J/cm^2)	Outcome
1	Lim et al,[12]	830 nm GaAsAl Diode, CW	59.7 mW	15 ,30 ,60 s	5 times Days -1,2,3,4,5	1.8	+
2	Turhani et al,[13]	670 nm GaAsAl Diode, CW	75 mW	30 s	once Day 1	2	+

3	Youssef et al, [14]	809 nm GaAsAl Diode, CW	100 mW	15 ,30 ,60 s	4 times Days -1,3,7,14	2	+
4	Fujiyama et al,[15]	CO_2 laser	2 W	10 s	Twice Day 1	2.5	+
5	Tortamano et al,[16]	830 nm GaAlAs diode CW	30 mW	15 s	once Day 1	2.5	+
6	Esper et al,[17]	660 nm InGaAlP, CW, 640nm, LED GaAlAs CW	0.03 W 0.10 W	10s	Once Day 1	4 4	-
7	Artes-Ribas et al,[18]	830-nm GaAlAs, CW	100 mW	20 s	Once Day 1	5	+
8	Bicakci et al,[19]	820 nm GaAlAs, CW	50 mW	5 s	Once Day 1	7.96	+
9	Doshi-Mehta et al,[20]	810 nm AlGaAs, CW	0.7 mw	10 s	5 times Days -1,3,5,7,14	8	+
10	Domı´nguez et al,[21]	830nm Ga-Al-As laser, CW	100 mW	20 s	Once Day 1	8	+
11	Eslamian et al,[22]	810 nm GaAlAs,CW	100 mW	20 s	Twice Day 1,2	2	+
12	Abtahi et al,[23]	904 nm GaAlAs laser, CW	200 mW	10s	5 times Days -1,3,5,7,14	6	-
13	Marini et al,[24]	910 nm GaAlAs laser, CW	160mW	20s	Once Day 1	5.4	+
14	Nóbregaet al,[25]	830 nm GaAlAs laser, CW	150mW	5s	Once Day 1	1	+
15	Kim et al,[26]	635nm GaAlAs laser, CW	6 mW 12.9 mW	15s	Daily twice 1 week		+
16	Heravi et al,[27]	810 nm GaAlAs laser, CW	200 mW	3s	6 times Days -1,4,7,11,15 ,28	2	-

17	Bayani et al,[28]	660 nm, InGaAlP diode laser, CW 810 nm GaAlAs diode laser	200 mW	5 s	Once Day 1	1.4 3.6	+
18	Sobouti et al ,[29]	632.8 nm He-Ne laser, CW	10 mw	40 s,80 s	Once Day 1	6	+
19	Furquim et al ,[30]	808 nm AsGaAl diode, CW	100 mW	10 s	Once Day 1	6	-
20	Dalaie et al,[31]	880 nm GaAlAs laser, CW	100 mW	10 s	Once Day 1	5	-
21	Almallah et al,[32]	830 nm GaAlAs laser, CW	100 mW	28s	Twice Day 1,2	4	+
22	Farias et al,[33]	810 nm AlGaAs , CW	100 mW	15 s	Once Day 1	2	+
23	Kochar et al,[34]	810 nm AlGaAs, CW	100 mW	10 s	Thrice Day1,3,5	5	+
24	Deshpande et al,[35]	904 nm GaAlAs laser,CW	10 W	30s	Once Day 1	6	+
25	Qamruddin et al,[36]	940-nm GaAlAs laser, CW	200 mW	20 s	Once Day 1	6	+
26	Hasan et al,[37]	830nm GaAlAs laser, CW	150 mW	15s	Once Day 1	2.25	-
27	Qamruddin et al [38]	940 nm GaAlAs laser, CW	100mW	10s	Once Day 1	7.5	+
28	Guram et al, [39]	810 nm GaAlAs laser, CW	0.2 W	5 s	4 times Day 7,14,24,31	5	+
29	Matarese et al,[40]	810nm GaAlAs laser, CW	1 W	10,20 s.	4 times Days 1,3,7,14	8	+

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30	Arshad et al,[41]	810 nm GaAlAs laser, CW	1W	30s	5 times Day1,2,3,4,5	4	+
31	Farias et al ,[42]	808 nm GaAlAs laser, CW	100 mW	15s	Once Day 1	2	+
32	Gupta et al,[43]	940 nm GaAlAs laser, CW	200 mW	20s	Once Day 1	4	+
33	Martins et al,[44]	810-nm GaAlAs, CW	100 mW	30s	Once Day 1	3	+
34	Song Wu et al,[45]	810-nm GaAlAs, CW	400 mW,	20s	5times 0 h, 2 h, 24 h, 4 ,7 days	2	+
35	Nahin et al,[46]	830 nm GaAsAl, CW	30 mW	10s	Once Day 1	2.5	+
36	Qamruddin et al,[47]	940-nm (Al-Ga-As), CW	100 mW.	3 s	Once Day 1	7.5	+
37	Antonio et al,[48]	980nm GaAlAs laser	1w	8-9 s	3 times Day 1- 2,4,6mins	6	+
38	Celebi et al,[49]	820nm GaAlAs laser, CW	50 mw	16s	Once Day 1	1.76	-
39	Nicotra et al,[50]	980nm GaAlAs laser, CW	1 w	10s	Thrice Day 1-10s,20s,30s	1	+
40	Prasad et al,[51]	980nm GaAlAs laser, CW	2.5 w	10s	Once Day 1	2.5	+
41	Hasan et al,[3]	830nm GaAlAs laser, CW	150mw	16s	Once Day 1	1.76	-

CW-Continuous wave mode, (+) Laser photobiomodulation was significantly more effective in controlling pain than control group, (-) No significant difference in pain control observed between laser photobiomodulation and control groups /Laser photobiomodulation was not effective in pain control