Complementary Therapies in Medicine 47 (2019) 102220

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

Photobiomodulation in acceleration of orthodontic tooth movement: A systematic review and meta analysis

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ARTICLE INFO

Keywords:
Low level laser therapy
Orthodontic tooth movement
Photobiomodulation

ABSTRACT

Background: Photobiomodulation therapy, a non invasive method with no adverse effects, has been used to accelerate tooth movement in orthodontia. However, the specific characteristics of laser settings used in studies documented have reported varied inconsistent conflicting results.
Objectives: We decided to undertake a systematic review to eliminate this inconsistency by quantifying the literature studies that indicated the link between photobiomodulation and acceleration of tooth movement and to assess if there is any association of photobiomodulation therapy in accelerating tooth movement.
Search strategy: We systematically searched for articles of existing literatures on Photobiomodulation therapy and acceleration of tooth movement over Cochrane library, Pubmed central, EMBASE, Scopus and Web of sciences from 2000 to 2017. Mesh search terms using various descriptors were used to identify the studies.
Search criteria: We included randomized control trial and clinical control trail studies that used Ga-Al-As diode laser and Oseeopulse laser with specific characteristics and company specifications, addressing relevant efficiency and safety outcomes.
Data collection and analysis: Eligible studies were reviewed and data was extracted on a standard from. We used Cochrane review manager software (Revman version 5.3) to assess the qualities of each included trials. Data were analyzed using an inverse variance method with random effects model effect.
Results: We observed a statistical significant difference between the photobiomodulation therapy compared to non laser group in the acceleration of tooth movement (Mean difference 0.59 (95%CI- 0.24 to 0.95) I^2 95%). However, these results need caution while generalizing in clinical practice due to the large amount of heterogeneity across the studies.
Conclusion: Findings of the current systematic review suggest a possible benefit with photobiomodulation therapy and tooth movement in orthodontia. However these findings need to be further validated in larger trials using specific standardized characteristics of laser settings to uniform the methodological design that can be used in routine clinical practice.

1. Introduction

The success of orthodontic treatment is primarily dependent on achieving rapid tooth movement and reducing the treatment duration. In clinical practice, the protracted orthodontic treatment period, often over 2 to 3 years time, is the frequent compliant of young adults who seek professional care. Researchers in the past have observed that 8–30% of patients refrain from treatment due to pain and long treatment time.[1] Various approaches such as application of intermittent resonance vibrations, drug injections of vitamin D, prostaglandins, osteocalcin around the alveolar sockets and surgical intervention like corticision were opted to overcome this issue. Although these methods

Abbreviations: LLLT, low level laser therapy; PDF, portable document full text format; USA, United States of America; PICO, population, intervention, comparsion and outcomes; RCT, randomized control trial; nm, nanometer; J/sq.cm, Joles per square meter; mW, megawatt

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https://doi.org/10.1016/j.ctim.2019.102220
Received 2 April 2019; Received in revised form 26 August 2019; Accepted 15 October 2019
Available online 16 October 2019
0965-2299/

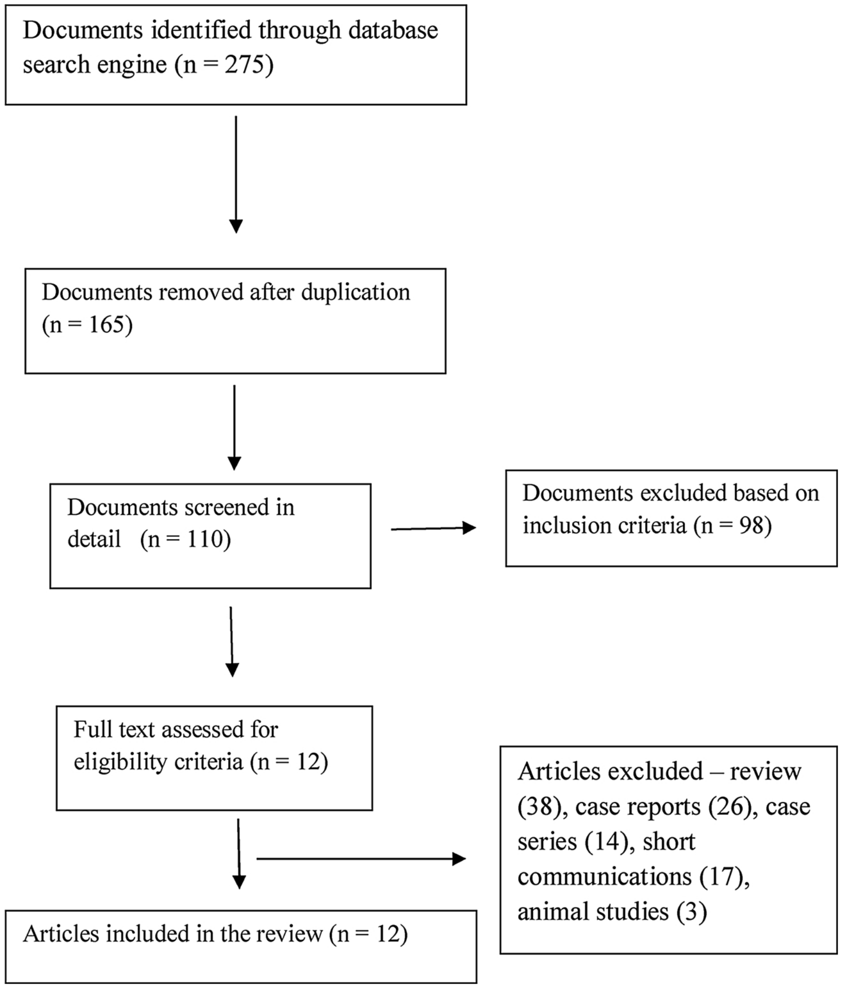

Fig. 1. Flowchart of the study identification.

were effective in accelerating the tooth movement, they were expensive, invasive approach with several adverse effects like pain and discomfort following injections and need for frequent applications to get the desired benefits. The use of less expensive, noninvasive approach using low level laser light therapy called Photobiomodulation therapy gained importance in orthodontics in yester years. It is also known as Light accelerated orthodontia (LAO) therapy or Low-level light therapy (LLLT) as it uses low energy light or laser in the red to near-infrared range of about 600–1000 nm.[2]

Photobiomodulation therapy is based on the principle of Arndt–Schulz law that states, “low dose of any substance or drug has a stimulating effect, whereas higher dose has inhibitory effect’.[3]

In the same manner, low doses of this therapy is an photonic radiation that causes cell stimulation by molecular and chemical mechanism wherein the photons are absorbed in the mitochondria by cytochrome-c oxidase and stimulate adenosine triphosphate (ATP) production and low levels of reactive oxygen species (ROS).[4] This anabolic effect further increases the acceleration of tooth movement by stimulating the proliferation and differentiation of different cell lineages like osteoblast, osteoclast, fibroblasts and PDL cells, thus imparting stimulatory effect for bone remodeling, collagen synthesis and revascularization.[5–9] The expression of basic fibroblast growth factor, macrophage colony stimulating factor, c-fms, tartarate-resistant acid phosphatase, matrix metallopeptidase-9, Cathepsin K and integrin contribute for this process.[10,11]

Several studies in the past have investigated the efficacy of photobiomodulation therapy in reducing pain[12–14] and on the acceleration of orthodontic tooth movement.[15] However, the specific uniform characteristics of different type of laser used and laser settings varied reporting conflicting results. In the view of these inconsistent findings, we decided to undertake a systematic review of literature to asses if there is any association of Photobiomodulation therapy and acceleration of tooth movement in orthodontia.

2. Materials and Methods

2.1. Protocol registration and search strategy

The current systematic review was registered as a protocol with International prospective register of systematic reviews (PROSPERO) platform bearing the ID no: **CRD42019119743**. The PICO framework (Population, Intervention, Comparison, Outcomes) was used.

P – Population being orthodontic cases

I – in vivo photobiomodulation therapy

C – Comparison between laser group and sham group/ non lased group

O- Acceleration of tooth movement

Focused guiding question formulated was “Does photobiomodulation therapy induces accelerated tooth movement during orthodontic treatment”?

2.2. Search strategy

We systematically performed a detailed electronic automated scientific literature search over Cochrane library (www.cochranelibrary.com), PubMed central, EMBASE, Scopus, and Web of Science (http://

scientific.thomson.com/products/sci/). The literature search was limited to studies published in English language only. Wherever necessary, we communicated with the authors for more information on relevant articles. We made use of various descriptors and Mesh(medical subject headings) terms, both individually and in combination, as follows: Laser Biostimulation; Laser Phototherapy; Laser Therapy, Low-Level; Laser Therapy, Low-Power; Low-Level Laser Therapy; Low-Power Laser Irradiation; Low-Power Laser Therapy; Photobiomodulation Therapy; Laser Irradiation, Low-Power; LLLT; Laser Irradiation, Low-Power; Orthodontic tooth movement; Acceleration of tooth movement. Finally we searched for Google, ProQuest, and OpenGrey for grey literature and removed the duplicate articles by using the End-Note software (End-Note X7®, Thomson Reuters, Philadelphia, USA)

2.3. Study selection and data extraction

We included all randomized control trail (RCT) and clinical control trail (CCT) studies that met the aim and objective of this systematic review. A total of ten RCT studies which compared the application of Ga-Al-As diode laser (laser /experimental group) with placebo group (control/ non laser group) with specific laser settings and two CCT studies which compared Osseoplulse LED (laser group) with placebo group (control/ non laser group) with specific laser settings were included. Review articles, short communications, case-reports, case series, letters to the editor, pilot study, animal studies and conference abstracts were excluded from the study design. The selection process of included studies was reported in PRISMA (Preferred reporting items for systematic review and Meta analysis) flow diagram. (Fig. 1) The included studies were further screened by two authors (IS & JH) for rechecking of data extracted using the below mentioned links: (www.cochranelibrary.com) & (http://scientific.thomson.com/products/sci/). Any disagreements were resolved by discussion and consensus. Thereafter, a table of ‘Characteristics of included studies’ was made that included the following information: first author, year of publication, location, study type, sample size, type of malocclusion, sample population involved, characteristics parameters of laser used i.e. energy density, power output, duration of application, dosage used, treatment and statistical outcomes (Tables 1 and 2).

2.4. Assessment of study quality

The finalized articles were assessed for their methodological quality by RK (statistician) who worked independently on each article based on the following criteria: random sequence generation, allocation concealment, blinding of intervention, Blinding of outcome assessment and other biases (Fig. 2).

2.5. Assessment of data synthesis & heterogeneity

We used Cochrane review manager software (REVMAN version 5.3. the Nordaic Cochrane centre, Copenhagen, Denmark) for quantitative analysis. For continuous data, we calculated mean difference with 95% confidence interval (CI). We performed a visual inspection of forest plot to assess the statistical heterogeneity. I^2 statistics was used to describe the percentage of variation across included studies due to heterogeneity. We planned to assess the publication bias using funnel plot. We conducted Meta analysis using the Rev man 5.3 and for continuous data we employed random assess model (Fig. 3).

Subgroup analysis

We intended to do subgroup analysis for application of Photobiomodulation therapy for

1. Maxillary arch 2. Both maxillary and mandibular arch

2.6. Sensitivity analysis

We intended to do sensitivity analysis to explore the impact of Ga-Al-As diode laser and Osseopulse LED Laser for acceleration of tooth movement. The risk of bias summary for all the included articles is shown in Fig. 2.

2.7. Results

The electronic search identified 275 studies and the titles and abstracts of these studies were examined for inclusion criteria. 12 potential and relevant studies were identified. The results of the search are illustrated in the PRISMA flow chart (Fig. 1). Reasons for exclusions are mentioned in PRISMA flow chart.

2.8. Included studies

We included 12 studies in this review and these studies were designed to assess effects of Photobiomodulation therapy on the acceleration of tooth movement. All studies obtained ethical approval prior to commencement of the studies and recruitment of participants. Fig. 1 shows the study selection process. A total of 226 participants were involved in the 12 studies. The participants had an extraction orthodontic treatment plan prior to laser treatment. Ga-Al-As diode laser was applied in 10 studies and osseopulse laser was applied in 2 studies.

3. Characteristics of the interventions

Cruz et al[16] applied Ga-Al-As diode laser of 5 J/sq cm energy density, 20 mW power output and 780 nm wavelength to maxillary arch with a total of 10 irradiations for 60 days time interval to accelerate tooth movement. Limpanichkul et al[17] assessed the tooth movement in maxillary arch by application of Ga-Al-As diode laser of 25 J/sq cm energy density, 100 mW power output and 860 nm wavelength to laser group at 1st, 2nd and 3 rd month adjacent to the mucosa. Kansal et al[20] applied Ga-Al-As diode laser of 4.2 J/sq cm energy density, 12 mW power output and 904 nm wavelength for 63 days time interval in maxillary arch. Ekizer et al[5] used Osseopulse laser of 20 mW power output and 618 nm wavelength for 3 months time interval in maxilla.Qamruddin I et al[24], in maxillary arch, utilized Ga-Al-As diode laser of 7.5 J/sq cm energy density, 100 mW power output and 940 nm wavelength applied at 3 week interval time to assess the acceleration of tooth movement. Youssef et al[18] in both maxillary and mandibular arch applied Ga-Al-As diode laser of 8 J/sq cm energy density, 100 mW power output and 809 nm wavelength for 14 days duration. Doshi et al[19] Ga-Al-As diode laser of 8 J/sq cm energy density, 100 mW power output and 810 nm wavelength in both the maxillary and mandibular arch for 3 month duration. Dalaie et al[22] applied Ga-Al-As diode laser of 5 J/sq cm energy density, 100 mW power output and 800 nm wavelength in both the maxillary and mandibular arch for,67 days duration. Heravi et al[21] assessed the tooth movement by applying Ga-Al-As diode laser of 21.4 J/sq cm energy density, 200 mW power output and 810 nm wavelength 56 days duration.

4. Characteristics of the outcomes

Outcomes assessed the primary objectives of assessing the acceleration of tooth movement. The outcome results were presented as continuous data describing the mean and standard deviation. No statistical test results to compare the intervention outcomes were clearly mentioned in either of the studies. We considered a clinically significant difference would be a difference that could potentially have an impact on the overall duration of treatment.

Risk of bias in included studies: Six of the included studies had a low risk of bias and remaining studies had unclear risk of bias in all of the domains. Further details of these assessments are given in the 'Risk of bias' table corresponding to each study in the Characteristics of included studies section. Overall ratings are also presented in the 'Risk of bias' summary in Fig. 3.

Table 1
Articles reviewed in the study.[3],[5],[16–25]

Author and year	Malocclusion type	Study type	Study design, blinding & Randomization	Study period	Age	Sample population and gender	Group of study
Cruz DR 2004	Lack of space, bimaxillary protrusion	RCT	Split mouth Not specified	Not mentioned	12-18 years	11 Gender not mentioned	Laser group Control group
W Limpanichkul 2006	Maxillary canine malocclusion	RCT matched pair clinical trial	Split mouth Double blind Block randomization was done	Notmentioned	20.11 + /-3.4 years	124-Male 8-Female	Laser Group Placebo Group
Youssef M 2008	Lack of space, bimaxillary protrusion	Prospective CCT	Split mouth Not mentioned	Not mentioned	14-23 years	15 Gender not mentioned	Laser group Control group
Doshi-Mehta G 2012	Not mentioned	RCT	Split mouth Single blind Randomization – incomplete block split mouth	Not mentioned	12-23 years	20 8-Male 12-Female	Control Group Experimental Group
Kansal A 2014	Lack of space, protrusion	Prospective CCT	Split mouth Triple blind Randomization- not mentioned	Not mentioned	Not mentioned	Total sample-10 Gender not mentioned	Laser Group Non laser Group
Heravi F 2014	Not mentioned	RCT	Split mouth Single blind	Not mentioned	22.1 + /-5.3	Total sample-20 3 –Male 17-Female	Laser Group Placebo Group
Dalaie K 2015	Not mentioned	Randomized control trail CCT	Split Mouth Double blind Randomization- in complete block randomization done using Microsoft Excel software	Not mentioned	20.1	Total sample- 12 Female -17 Male -3	Laser Group Control Group
Abdullah Ekizer 2016	Malocclusion type not mentioned	Randomized control trail	Double blind, split mouth design Randomization- coin toss method	December 2013 to February 2015.	16.77_1.41 years	Total sample – 20 Females- 13 Males- 7	Laser Group Non laser Group
Mohammad Moaffak 2017	Crowded maxillary incisors according to Little's irregularity index	Randomized control trail	Two-arm, parallel-group Randomization- paper chit method	July 2015 and March 2016.	16 and 24 Years	Total sample-26 Gender not mentioned	Laser Group Control Group
Irfan Qamruddin 2017	Angle Class II Division 1 malocclusion	Randomized clinical trial	Single-blind, split mouth Randomization is done by flipping a coin	Not mentioned	19.8 6 3.1 years	Total sample –22 Females- 11 Males- 11	Laser Group Placebo Group
Guneet Guram 2018	Simple Class I bimaxillary protrusion cases	Randomized control trail	Not mentioned Randomization- not mentioned	April 2013 and July 2016	17–24 years,	Total sample- 20Females- 12 Males- 8	Laser Group Control Group
Nour Al Okla 2018	Maxillary anterior crowding	Randomized clinical trail	Double blind Randomization- not mentioned	Not mentioned	Not mentioned	Total sample- 38 Gender not mentioned	Treatment group Placebo group

Table 2
Characteristics of the low level laser used for the acceleration of tooth movement.[3,5,16–25]

Author	Type of laser used	Energy density	Power output	Wave length	Accelerated tooth movement	p value	Grading
Cruz DR	Ga-Al-As diode laser (Twin Laser, MM Optics Ltda., Sa˜o Carlos, SP, Brazil),	5 J/sq.cm	20 mW	780 nm	Yes	$p < 0.001$	Highly significant
W Limpanichkul	Ga-Al-As diode laser (Top Laser 250 SIR 100, Medical Innovation, France)	25 J/sq.cm	100 mW	860 nm	No	$p = 0.77$	Non significant
Youssef M	Ga-Al-As diode laser	8 J/sq.cm	100 mW	809 nm	Yes	$p < 0.05$	Significant
Doshi-Mehta G	Ga-Al-As diode laser	8 J/sq.cm	100 mW	810 nm	Yes	$p = 0.000$ to 0.0381	Highly significant
Kansal A	Ga-Al-As diode laser (ORALIA Dental Products, D-7750 Konstanz, Germany),	4.2 J/sq.cm	12 mW	904 nm	Yes	$p = 0.34$ to 0.69	Non significant
Heravi F	Ga-Al-As diode laser	21.4 J/sq.cm	200mW	810 nm	No	$p > 0.05$	Non significant
Dalaie K	Ga-Al-As diode laser (photo lase III, Brazil)	5 J/sq.cm	100 mW	800 nm	No	$p = 0.45$	Non significant
Abdullah Ekizer	LLLT OsseoPulse	20 mW/cm2	Not mentioned	618 nm	Yes	$p < 0.001$	Highly significant
Mohammad Moaffak	Ga-Al-Aslaser	2.25 J/ cm^2	150 mW	830 nm	Yes	$p < 0.001$	Highly significant
Irfan Qamruddin	Ga-Al-As Laser (iLas; Biolase, Irvine, Calif)	7.5 J/ cm^2	100 mW	940 nm	Yes	$p < 0.05$	Significant
Guneet Guram	Ga-Al-As laser Photon Lase Plus unit (DMC, São Carlos, São Paulo, Brazil).	5 J/cm^2	0.2 W	810 nm	Yes	$p > 0.05$	Non significant
Nour Al Okla	OrthoPulse®(Vancouver, BC, Canada)	0.065 J/cm2	Not mentioned	850 nm	Yes	$p = 0.028$	Non significant

4.1. Allocation

Selection bias can be minimized when participants and study personnel cannot foresee the upcoming assignment. AlSayed Hasan MMA,[23] Dalaie K,[22] Ekizer A,[5] Qamruddin I,[24] Kansal A[20] and Limpanichkul W[17] clearly described the randomization process; however the allocation concealment was not described by Dalaie K,[22] Qamruddin I[24] and Kansal A.[20] The remaining studies showed unclear risk of bias.

4.2. Blinding

Performance bias can be reduced by blinding both participants and study personnel to the type of intervention allocated. Studies by Doshi-Mehta G,[19] Ekizer A,[5] Kansal A[20] and Limpanichkul W[17] showed low risk of bias whereas studies conducted by Cruz DR,[16] Okla NA,[25] Youssef M,[18] Dalaie K,[22] Guram G,[3] Heravi F[21] and Qamruddin I[24] showed unclear risk of bias. One study by AlSayed Hasan MMA[23] revealed high risk of bias

5. Incomplete outcome data

None of the studies revealed attrition bias. All of the studies showed complete outcome data with clear description of study data. Hence included studies revealed low risk of bias.

6. Selective reporting

All the studied have reported the pre-stated outcome in the methods. Therefore we have judged this domain as low risk of bias.

7. Effect of intervention

In the maxillary group, there is statistical significant result with MD 0.56(95% CI 0.06–1.06) whereas in both maxillary and mandibular group, there was no statistical significant result with MD 0.59(95%CI −0.13to 1.30)

The overall result shows that laser group with Photobiomodulation therapy has better affect on tooth acceleration (0.59 mm) with 95% confidence interval (95%CI 0.24 to 0.97).

We have performed a subgroup analysis to investigate the reason for heterogeneity by comparing the studies provided with change score vs. endpoint score. However, it neither didn't change our results nor reduced the level of heterogeneity. Since studies have used a various power outputs, which may be have likely produced very large effects in some studies.

8. Subgroup analysis result of maxillary arch

Cruz et al[16] in their RCT, Split mouth design included 11 cases of bimaxillary protrusion and applied Ga-Al-As diode laser of 5 J/sq cm energy density, 20 mW power output and 780 nm wavelength to lased group. A total of 10 irradiations were done at 60 days time interval. The final mean difference was 4.39 ± 0.27 in lased group and 3.3 ± 0.24 in control group showing highly significant difference with $p < 0.001$ indication acceleration of tooth movement.

Limpanichkul et al[17] in their RCT, Split mouth, double blind design included 12 cases (4 M, 8 F) of maxillary canine malocclusion and divided the maxillary quadrant into laser group and placebo group. They applied Ga-Al-As diode laser of 25 J/sq cm energy density, 100 mW power output and 860 nm wavelength to laser group at 1st, 2nd and 3 rd months adjacent to the mucosa. The final mean difference was 1.29 ± 0.21 in lased group and 1.24 ± 0.21 in placebo group showing highly significant difference with $p = 0.77$ indication no acceleration of tooth movement.

Kansal et al[20] in their prospective CCT, Split mouth, design included 10 cases of maxillary protrusion cases, divided the maxillary arch into

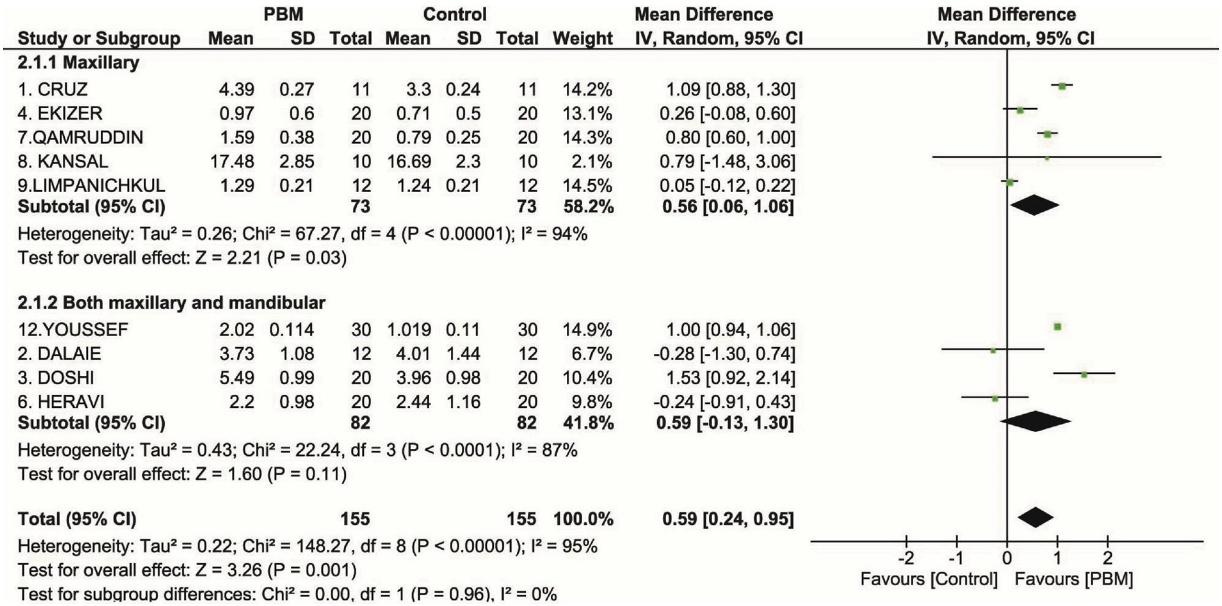

Fig. 2. Forest Plot- Photobiomodulation in acceleration of orthodontic tooth movement.

laser group and non laser group and applied Ga-Al-As diode laser of 4.2 J/sq cm energy density, 12 mW power output and 904 nm wavelength. A total of 10 irradiations at 1st, 3 rd, 7th, 14th, 21st, 28th, 35th, 42th, 49th, 56th, and 63rd day was applied. The final mean difference was 17.48 ± 2.85 in lased group and 16.98 ± 2.3 in non laser group showing no significant difference with $p = 0.34$ indication no acceleration of tooth movement. This difference could be attributed due to variations in laser setting in which 4.2 j/sq.cm, 12mw and 903 nm wavelength was used. When compared to other studies, this study showed variations in all 3 parameters (power output, energy density and wavelength) of laser settings in total of 10 samples. One more reason could be the small sample size and the density of maxillary bone that could have contributed to non significant results. In addition, this study goes in accordance to Arndt- Schulz law and thus shows inhibitory effect at high dose.

Ekizer et al[5] in their RCT design included 20 cases (M-7, F-13) of maxillary cases and divided into laser group and non laser group utilized Osseopulse laser of 20 mW power output and 618 nm wavelength applied at 1st, 2nd and 3rd month showed highly significant $p < 0.001$. The final mean difference was 0.97 ± 0.6 in lased group and 0.71 ± 0.5 in non laser group with acceleration of tooth movement.

Irfan et al[23] in their RCT, Single blind, Split mouth design included 22 cases (M-11, F-11) and utilized Ga-Al-As diode laser of 7.5 J/sq cm energy density, 100 mW power output and 940 nm wavelength applied at 3 week interval time to laser group. The final mean difference was 1.59 ± 0.38 in lased group and 0.79 ± 0.25 in placebo group showing no significant difference with $p = 0.34$ indication no acceleration of tooth movement.

9. Subgroup analysis result of maxillary and mandibular arch

Youssef et al[18] in their prospective CCT, Split mouth design included 15 cases and divided both maxillary and mandibular arch into laser group and control group. They applied Ga-Al-As diode laser of 8 J/sq cm energy density, 100 mW power output and 809 nm wavelength in both the maxillary and mandibular arch for 3, 7, 14 day duration. The final mean difference was 2.02 ± 0.114 in lased group and 1.019 ± 0.11 in control group showing highly significant difference with $p < 0.05$, indication acceleration of tooth movement.

Doshi et al[19] in their RCT, Single blind, Split mouth design included 20 cases(M-8, F-12) and divided into experimental group and control group. They applied Ga-Al-As diode laser of 8 J/sq cm energy density, 100 mW power output and 810 nm wavelength in both the maxillary and mandibular arch for 3 month duration. The final mean difference was 5.49 ± 0.99 in experimental group and 3.96 ± 0.98 in control group showing highly significant difference ($p < 0.03$), indicating acceleration of tooth movement.

Dalaie et al[22] in RCT, Double blind, Split mouth design included 12 cases(M-3, F-13) and divided maxillary and mandibular arch into laser group and control group. They applied Ga-Al-As diode laser of 5 J/sq cm energy density, 100 mW power output and 800 nm wavelength in both the maxillary and mandibular arch for 3, 7, 30, 33, 60, 63, 67 day duration. The final mean difference was 3.73 ± 1.08 in laser group and 4.01 ± 1.44 in control group showing no significant ($p = 0.45$) indication no acceleration of tooth movement.

Heravi et al[21] in their RCT, Single blind, Split mouth design included 20 cases (M-3, F-17) and divided into laser group and placebo group. They applied Ga-Al-As diode laser of 21.4 J/sq cm energy density, 200 mW power output and 810 nm wavelength in both the maxillary and mandibular arch for 4th, 7th, 11th, 15th, 56th day duration. The final mean difference was 2.2 ± 0.98 in laser group and 2.44 ± 1.16 in placebo group showing no significant ($p > 0.05$) indication no acceleration of tooth movement.

10. Discussion

The identification of Photobiomodulation therapy as an effective method when compared to previous expensive, invasive and discomfort methods such as local drug injections of prostaglandins and osteocalcin in the alveolar socket[7,26] and ultrasound application[16,27] was a question of debate. Photobiomodulation therapy, being a noninvasive method, accelerates tooth movement in orthodontia by increasing the number of osteoclasts for bone remodeling and exerting stimulatory effect for collagen synthesis and revascularization.[5] At cellular level, this therapy initiates a photochemical reaction wherein light energy of about 610–850 nm wavelength is absorbed by the cellular photoreceptors generating an electromagnetic field which in turn increases cytochrome C oxidase enzymatic activity in the mitochondrial respiratory chain, thus pumping ATP.[2,7] In addition, it facilitates vasodilatation, proliferation, differentiation of cell lineages of osteoblastic and periodontal ligament cells; wound healing process by stimulating the fibroblasts and inhibit the transmission of pain signals by imparting analgesic effect.[7–9]

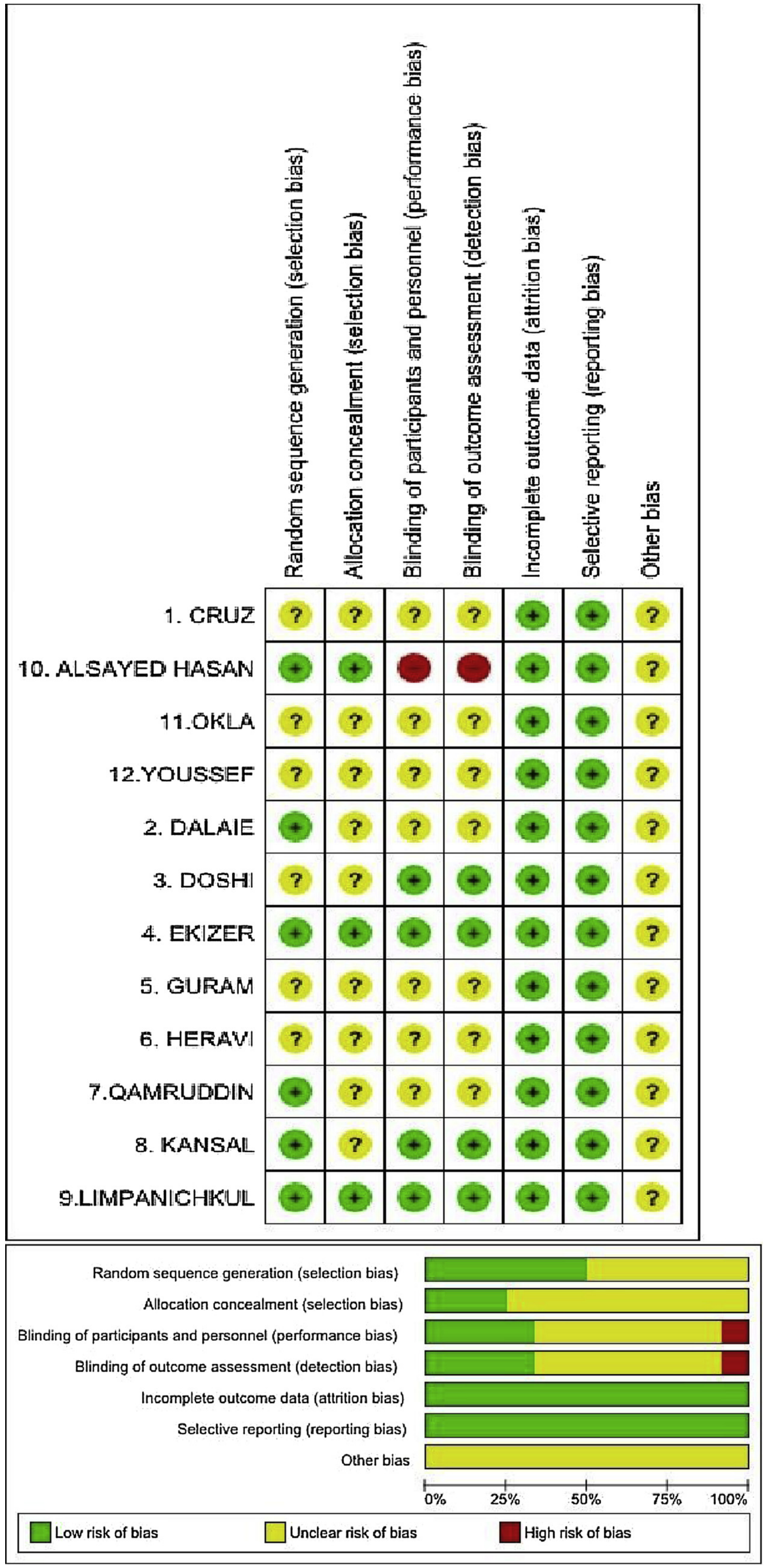

Fig. 3. Risk of Bias of the studies included.

Several studies conducted in the past using Photobiomodulation therapy for acceleration of tooth movement showed conflicting results and heterogeneity due to difference in laser characteristics like wavelength, power output etc. Based on this, the present discussion is as follows:

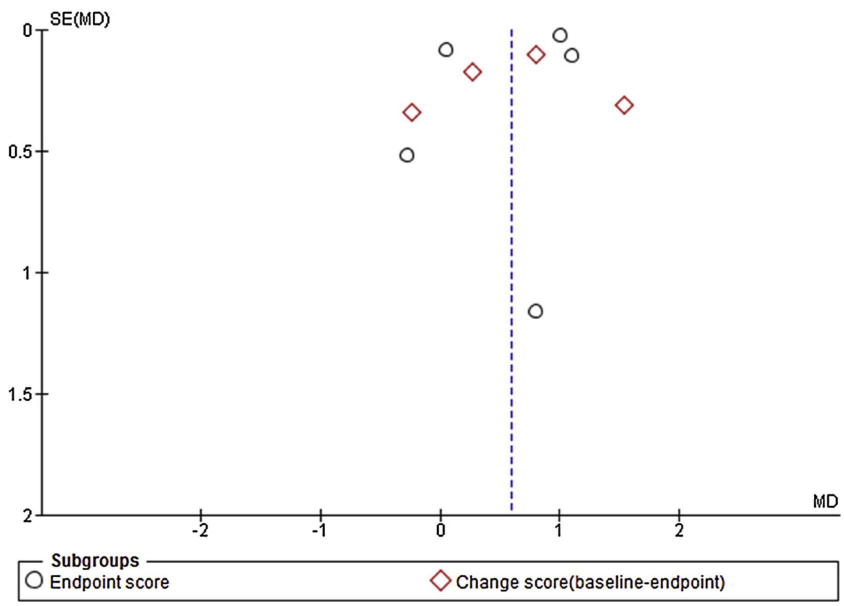

Fig. 4. Funnel Plot.

10.1. Wavelength

80% of studies showed a laser wavelength ranging from 750 to 900 nm [3,5,16,17,18,19] and the higher the wavelength, the tooth movement in these studies was not possible. This goes in accordance to Arntz Schutz law which stated that higher the does, the laser therapy showed inhibitory effects, except for one study conducted by Irfan Qamruddin et al[24] which showed highly significant results with 940 nm. This raises a hypothesis to be proved in further studies to see if the higher wavelength laser therapy is leading to tooth movement and possibly rejecting the null hypothesis. Study conducted by Ekizer et al[5] using photobiomodulation osseo pulse laser of 618 nm showed highly significant results with a p value $p < 0.001$. This again goes in accordance to Arntz Schutz law (lower dosages have stimulatory effects) (Table 2).

10.2. Energy density

Most of the studies used an energy density of about 4.2–8 J/sq.cm in which few studies showed a favorable effect[16,18,19,20,22] whereas studies conducted by Guram et al[3] and Kansal et al[20] utilizing the same energy density showed non significant results. One more study conducted by Limpanichkul et al[17] inferred that the energy density of about 25 J/sq.cm could not accelerate tooth movement. Also Heravi et al[21] used an energy density of about 21.5 J/ sq.cm and showed no significant results. Study conducted by Mohammad Moaffak[23] used 2.25 J/sq.cm and showed highly significant results. This concludes that energy density of less than 4.2 J/sq.cm can also produce significant results and hence further studies using lesser energy density specifications should be conducted to produce definite results (Table 2).

10.3. Power output

It was also observed that based on power output, 20–100 mW gave a positive result [16,18,19,22] whereas 200 Mw[21] gave no effect on tooth movement (Table 2).

From these points, one can conclude that Ga As Al didode laser with wavelength of 740–900 nm, energy density of 2.25–8 J/sq.cm and 20–100 mW power output can accelerate tooth movement in orthodontia.

Due to high heterogeneity of reviewed studies (Fig. 4), the authors recommend conducting more number of studies using specific characteristic of laser and standardize the procedures which can be more precise and authentic.

11. Conclusion

The results of the current review showed heterogeneity in all these studies. The reason for the heterogeneity could be the characteristics of laser used i.e. wavelength, power output, energy density, duration time of application of laser and area of intervention (maxillary or mandibular arch). Further studies should evaluate the hypothesis if the amount of bone density and vasculature can influence the laser therapy in accelerating tooth movement. Given using the random effect model accounting the variability in the data, we were still able to obtain statistically significant results to suggest that "**PBM may have a possible benefit**" in the acceleration of orthodontic tooth movement.

Source of support

None.

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