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Assessment of the effect of frequency of low-level laser therapy exposure at different intervals on orthodontic tooth movement – A systematic review and meta-analysis

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Abstract

OBJECTIVE: To assess the optimal intervals of exposure of low-level LASER therapy (LLLT) that would optimally accelerate orthodontic tooth movement. Second objective was to quantitatively analyze the difference in the time taken for alignment of anterior teeth with and without the application of LASER.

MATERIALS AND METHODS: PROSPERO database registry was done (CRD42020196472) and review was conducted based on PRISMA guidelines. A search was systematically conducted in five major electronic databases without restrictions up to June 2020 along with a hand search of selected journals. The quality of evidence was assessed using the Grading of Recommended Assessment, Development, and Evaluation tool, risk of bias using Cochrane risk of bias tool, and meta-analysis was carried out using RevMan 5.4 software.

RESULTS: Ten randomized controlled trials which met the inclusion criteria were evaluated and tabulated. A random-effects meta-analysis demonstrated that there is a statistically significant increase in the orthodontic tooth movement when patients were exposed to minimum of four intervals of LLLT in the first month, at P =0.03 by a standard mean difference of 0.46 mm with an overall heterogeneity of I^2 = 0% at 95% confidence interval. There was a statistically highly significant reduction in the number of days taken for alignment of anterior teeth with the application of LASER (P < .00001).

CONCLUSION: Application of LLLT for minimum of four irradiations in the first month has yielded better results in accelerating orthodontic tooth movement than application of LLLT once a month.

Keywords:

Accelerated orthodontic tooth movement, frequency of LLLT exposure, LASER, LLLT

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Introduction

Orthodontic tooth movement (OTM) is defined as an adaptive biological response as the result of periodontal ligament remodeling during and after the application of forces which stimulates bone resorption on the compression site and bone deposition on the tension side, finally reorganizing the periodontal ligament.[1]

Numerous modalities have been used to accelerate OTM; few of them being mechanical vibration, corticotomy, piezocision, pharmacological adjutants, and low-level LASER therapy (LLLT).[2,3] Literature shows that LLLT has been effective in inducing remodeling processes in both

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soft and hard tissue due to cellular absorption of LASER by the target tissue, which causes the intracellular signaling activation resulting in accelerated OTM and reduced orthodontic treatment duration.[4-6]

Although the use of LLLT to accelerate OTM has been assessed with regard to wavelength, an evaluation of the exposure at different time intervals has not been assessed qualitatively and quantitatively. There are studies proving the reduction in time duration taken for alignment of anterior teeth, yet the same has not been quantitatively analyzed. Therefore, the aim of this systematic review and meta-analysis is to evaluate the effect of variation in frequency of application of LASER on the rate of OTM and also to analyze the duration taken for alignment of anterior teeth in control and test group by means of a meta-analysis.

Materials and Methods

Protocol and registration

The study protocol for the systematic review was registered with PROSPERO (International Prospective Register of Systematic Reviews) REG NUMBER- CRD42020196472 and was carried out referring to the Cochrane Handbook for Systematic Reviews of Interventions.[7]

The methodology used in this systematic review was based on the PRISMA instructions, to identify the relevant article for review.[8]

A guiding question formulated was, "what is the effect of variation in the number of irradiation appointments of LLLT in accelerating OTM?"

Selection criteria

The studies which satisfied the following eligibility criteria were included in the systematic review:

1. Participants: Orthodontic patients exposed to low-level LASER for the purpose of accelerating tooth movement.
2. Intervention/exposure: LLLT during orthodontic mechanotherapy/space closure.
3. Comparison: Similar group/quadrant without application of LASER.
4. Outcome measures: Difference/acceleration in tooth movement with variation in exposure intervals of LLLT.
5. Study design: Randomized control trial (RCT).

Exclusion criteria

1. Nonrandomized trials.
2. Animal studies.
3. High-level LASER and light emitting diode.
4. Articles, reviews, case reports, opinions, columns in publications, letters, abstracts, and pilot study.
5. Study without adequate data.
6. Any studies which used other interventions along with LLLT (e.g., LLLT after corticision).

Information source and search strategy

Based on PRISMA guidelines, a search was conducted in the following major five electronic databases: PubMed, Scopus, SciELO, Cochrane, and Google scholar using the strategy given in Table 1. Grey literature was sought from Greynet and Ovid. The search was conducted till June 2020, did not have any language restrictions, and unpublished data were not taken into consideration for the review.

Study selection

Initially, all the references were exported to Zotero Desktop 5.0.87 software, to track potential duplicate records. Subsequently, titles and abstracts were read in detail to exclude articles which were out of the scope of research. At this stage, literature reviews, case reports, and experimental surveys with animals were also excluded. Full-text analysis of articles, whose title and abstract did not present sufficient information, were downloaded and analyzed to decide their eligibility for inclusion. Full texts of all the selected articles were downloaded and the details were tabulated in a PRISMA flowchart [Figure 1].

Data extraction and synthesis

Data were independently collected by five reviewers and basic details about articles such as type of LASER, its characteristics, clinical findings, and outcome of study were done using a data collection form.[9-18] Finally, all the data were compared for accuracy and any conflict was resolved through re-examination of the original study and discussion among all the reviewers until consensus and a study characteristics table was tabulated [Table 2].

Table 1: Electronic database and the applied search strategy

Database	Search strategy
PubMed -147	(low-level LASER therapy) AND (low-intensity LASER) AND (LLLT) AND (orthodontic tooth movement)
Cochrane library- 47	(low-level LASER therapy) AND (low-intensity LASER) AND (LLLT) AND (orthodontic tooth movement) AND (randomized controlled trial [RCT])
SciELO- 0	(low-level LASER therapy) AND (low-intensity LASER) AND (LLLT) AND (orthodontic tooth movement) AND (randomized controlled trial [RCT]) AND (cold-soft diode LASER) AND (GA-AL-AS LASER)
Google scholar -50	Low-level LASER therapy AND low-intensity LASER AND LLLT AND orthodontic tooth movement AND randomized controlled trial (RCT) AND diode LASER AND "GA-AL-AS" LASER
Science direct- 24	(low-level LASER therapy) AND (low-intensity LASER) AND (LLLT) AND (orthodontic tooth movement) AND (randomized controlled trial [RCT])

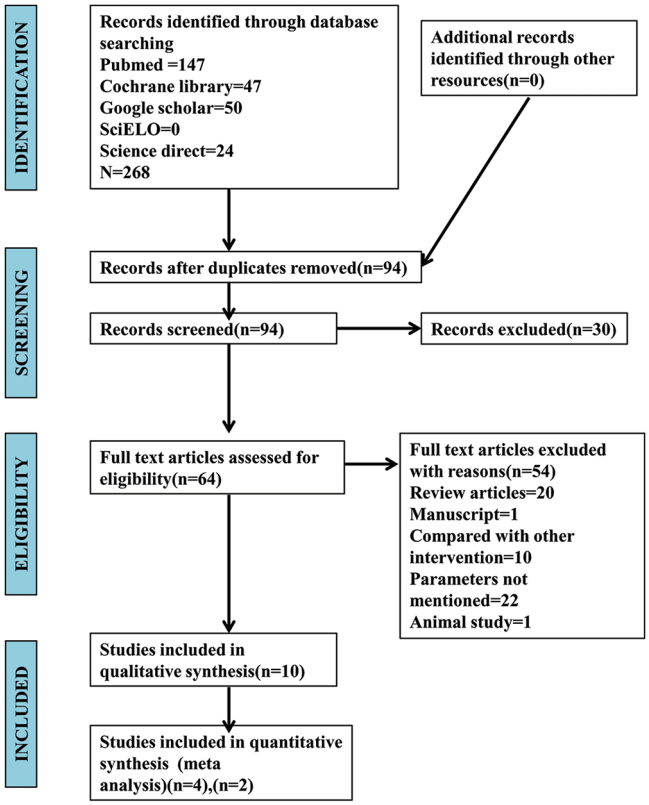

Figure 1: PRISMA flowchart

Quality assessment

Quality assessment of the selected articles for a systematic review was performed using the Grading of Recommended Assessment, Development, and Evaluation tool[19] [Table 2].

Risk of bias in individual studies

Finalized articles were thoroughly evaluated for their quality and potential risk of bias based on an evaluation adopted from Cochrane risk-of-bias tool for randomized trial RoB-2 tool.[20]

To evaluate the overall risk of bias, the analysis of each criterion was combined or the final assessment was given [Table 3]. For each criterion, the low, unclear, or high risk of bias was awarded.

Summary measures and approach to synthesis

Random-effects meta-analysis of the mean difference in the rate of canine retraction during LLLT exposure at two different intervals was carried out using Review Manager (RevMan) version 5.4. Four randomized clinical trials were statistically evaluated separately with a subgroup analysis and significance established at P <.05.[13,14,17,18] Results of the analyses are presented graphically with forest plot after comparison of the study design and methodology to evaluate the clinical heterogeneity of the studies [Figure 2].

Two randomized clinical trials were statistically analyzed, and significance established at P < .05.[9,11] Results of the analyses are presented graphically with forest plot after study design and methodology heterogeneity were checked [Figure 3].

Results

Study selection and characteristics

The literature search done is given in Table 1. Of four electronic databases, a total of 268 articles were evaluated, from which 64 full-text articles were examined in detail. Finally, 10 studies that satisfied the eligibility criteria were taken for final reviewing and quality analysis; and four RCTs were selected for quantitative data extraction to assess the rate of canine retraction and two RCTs were selected for quantitative data extraction to analyze the reduction in duration of alignment of anterior teeth [Figure 1].

In this study, 10 experimental studies involving LLLT were evaluated and tabulated with different aspects like type of LASER used, their wavelength, power output, and point of irradiation and interval [Table 4].

Risk of bias within studies

Risk of bias for each study is presented in Table 3. Of the 10 studies, five studies were found to have low risk and five studies had moderate risk of bias.

Results of Individual Studies and Meta-Analysis

Of the 10 studies which were evaluated for evidence, eight studies showed accelerated tooth movement with LLLT [Table 2]; an increased frequency of application with many intervals of exposure showed reduced treatment time than the control group. Thus, the result showed that LLLT can be effectively used in accelerating the OTM and reduce the treatment time effectively.

Effects of LLLT on accelerated OTM were drawn based on the criteria for assessing study quality. While comparing the parameters of the LASER used in different studies, majority of the studies commonly used Ga-Al-As LASER in a continuous wave mode and with the wavelength ranging from 618 nm to 980 nm which is infrared in nature [Table 2].

LASER's power output between 20 and 150 mW gave a positive result, whereas anything lower or higher had no effect on tooth movement, which points that a very high-power output could be the reason for a negative outcome in the other two studies that showed insignificant OTM when exposed to LLLT.[12,17]

Table 2: Study characteristics and quality assessment

LLlt exposure during alignment and levelling (nonextraction)							
Studies	**Study design**	**Participants**	**Intervention**	**Experimental group**	**Control group**	**Outcome**	**(Quality assesment)**
Amer z. Nahas *et al*. (2017)[9]	Rct	Patients (n=40) with lower Anterior crowding, who were treated with self- ligating orthodontic brackets.	Treated with extraoral Infrared light therapy for 20 min daily.	(*n*=20) patients who were subjected to extra oral laser therapy.	(*n*=20) controlgroup Not subject tolaser.	The use of photobio Modulation for 20 min daily at a wavelength of 850 nm, might reduce the time required to resolve lower anterior crowding.	High
Gianluigi caccianig *et al* (2017)[10]	Rct (pilot Study)	Patients (n=36) who Underwent orthodontic treatment.	A single monthly Administration of lllt was performed intra orally using a diode laser (980 nm, 1 w, continuous wave, total Energy\density=150j/cm^2; doctor smile-lambda spa).	Fixed mechanotherapy and lllt (*n*=18).	Fixed mechanotherapy only (*n*=18).	The results of this pilot study suggest that the administration of lllt in 980 nm for a single monthly administration for specific time intervals might significantly increase the efficiency of orthodontic treatment during dental alignment.	Moderate (Pilot study)
LLlt exposure during alignment and levelling (extraction)							
Studies	**Study design**	**Participants**	**Intervention**	**Experimental group**	**Control group**	**Outcome**	**(Quality assesment)**
Mohammad moaffak a. Alsayed hasan *et al*. (2017)[11]	Rct (parallel group design)	26 Patients aged between 16 and 24 years on whom extraction of two first premolars were done.	Two groups underwent treatment with fixed appliance. One group with Laser application at 830 nm for 3,7,14, and every 15 Days and another group Without laser.	Laser application at 3,7,14, and every 15 days following premolar extraction 830-nm Wavelength ga-al-as semiconductor laser	Control group with fixed appliance Following premolar extraction.	Increase in otm after lllt application at 830 nm for 3,7, and 14 days for 1st month And every 15 days from second month until end of leveling and alignment.	High
LLlt exposure during canine retraction (extraction)							
Studies	**Study design**	**Participants**	**Intervention**	**Experimental group**	**Control group**	**Outcome**	**(Quality assesment)**
Irfan qamruddin *et al*. (2017)[12]	Single Blinded rct	Twenty-two patients (11 Male, 11 female; mean age, 19.8±3.1 Years) with angle class ii division 1 malocclusion were recruited for this split- mouth clinical trial.	LLlt applied during Orthodontic treatment at 3 weeks interval time.	A gallium-aluminum- Arsenic diode laser 940 nm in a continuous mode (energy density,7.5 J/cm 2/point; diameter of optical fiber tip, 0.04 Cm 2) was applied at 5 points buccally and palatally around the canineroots	Opposite side of arch Considered as placebo	Canine retraction was Significantly greater in the expiremnetal group than control when laser at 940 nm was applied at 3 weeks interval.	High
Limpanichkul w *et al*. (2006)[13]	Rct	*n*=12 young adult patients (Four males and eight females; mean age 20.11±3.4 Years) who required retraction of maxillary canines using coil springs with fixed edge wise appliance.	LLlt (ga-al-as) at the Surface level (25 j/cm^2) was applied for 3 days once in a month for a total of four months.	LLlt was applied on The mucosa buccally, distally and palatally to the canine on the test side.	Pseudo-application On the placeboside.	There was no significant Difference of means of the canine distal movement between the lllt side and the placebo side, for any time period when lllt at 860 nm was applied for 3 days once in a month.	High

Contd...

Table 2: Contd...

LIlt exposure during canine retraction (extraction)							
Studies	**Study design**	**Participants**	**Intervention**	**Experimental group**	**Control group**	**Outcome**	**(Quality assesment)**
Gauri doshi-mehta *et al*. (2012)[14]	Rct	Twenty patients requiring Extraction of first premolars were selected for this study.	The laser regimen was Applied on days 0, 3, 7, and 14 in the first month, and there after on every 15th day until complete canine retraction was achieved.	The experimental side Received infrared radiation from a semiconductor (aluminium-gallium-arsenide) diode laser with a wavelength of 810 nm.	Opposite side of arch Considered as placebo.	An average increase of 30% in the rate of tooth movement was observed with the low- intensity laser therapy when applied for 4 alternate days for one month and every 15th day thereafter. Pain scores on the experimental sides were significantly lower compared with the controlsides.	Moderate (Propective study)
Abdullah ekizer *et al*. (2016)[15]	Rct (split mouth design)	20 Patients (13 girls, 7 boys). Included patients who had extraction of maxillary first premolars. Mini-screws were placed between maxillary First molars and second premolars on both sides as Anchorage units.	Mini screw on both sides ofmaxillary arch, lptapplication on one quadrant for 20 minutes once a day for a total of 21 days.	Application on one side following premolar extraction lpt was applied with an energy density Of 20 mw/ cm2 over a Period of 21 successive days (20 Minutes per day).	Split mouth with non Lpt side following premolar extraction.	Increase in otm on the experimental side when Lpt applied at 618 nm for 20 minutes once a day for a total of 21 days.	High
Alissa maria varella *et al*. (2018)[16]	Rct (split mouth Design)	10 Patients (6 female, 4 male) Aged 14 to 25 years, whose Maxillary first premolars Were extracted.	Experimental canine distalized with laser Therapy applied for 10 secs For 3 consecutive days at The start of canine Retraction then at 4 & 8 Weeks later, control canine Distalized without laser.	Canine received low laser therapy with distalization Gallium-aluminum-arsenide Semiconductor diode laser (Wavelength of 940 nm).	Control group had canine With Distalizing Force.	Light force with laser therapy at 940 nm applied For 10 secs for 3 Consecutive days at the Start of canine retraction Then at 4 & 8 weeks Increased otm levels of Il1b in gcf.	Moderate (Low sample size And outcomenot Conclusive)
Sevin erol Üretürk *et al*. (2017)[17]	Rct (split mouth design)	15 Patients maxillary first premolars of the 15 angle class ii division i patients (12-19 Years old) were Extracted.	Right and left canines, one side irradiated with laser as five doses from buccal and Palatal side on day 0,3,7,14,21,30, 33,37,60,63,67.	Laser irradiation along with clinical procedures on one side (gaalas) using a diode Low-level laser with a Wavelength of 820 nm.	Without irradiationalong with Clinical Procedures.	Increased otm on the laser irradiation side at 820 nm as five doses from buccal and Palatal side on day 0,3,7,14,21,30, 33,37,60,63,67.	Moderate Low sample size and outcomenot Conclusive

Contd...

Table 2: Contd...

LIlt exposure during canine retraction (extraction)							
Studies	**Study design**	**Participants**	**Intervention**	**Experimental group**	**Control group**	**Outcome**	**(Quality assesment)**
Dipika mistry *et al*. (2020)[18]	Rct (triple-blinded)	22 Patients (15 female, 7 Male; aged 13-25 years) requiring bilateral Maxillary first premolar Extractions.	Right side of each patient Was randomized to either an experimental lllt Group or sham control Group. The lllt group Received laser application Every 4 weeks	Ga-a1-as diode laser with 808 Wavelegnth on experimental side on day 0, 28, and 56.	Sham laser on Control group.	Application of lllt at 808 nm every 4 weeks did Not increase otm.	High

Table 3: Risk of Bias for Randomized Control Trials using Cochrane tool

Studies	Random sequence generation	Allocation concealment	Blinding of participants & personnel	Blinding of outcome assesment	Incompltete outcome data	Selection of reported result	Overall risk of bias
Amer z. Nahas *et al*. (2017)[9]	Low	Low	Low	Unclear	Low	Low	Good
Gianluigi Caccianiga *et al*. (2017)[10]	Low	Low	Unclear	Unclear	Unclear	Low	Fair
Mohammad moaffak a. Alsayed hasan *et al*. (2017)[11]	Low	Low	Low	Unclear	Low	Low	Fair
Irfan qamruddin *et al*. (2017)[12]	Low	Unclear	Low	Low	Low	Low	Good
Limpanichkul W *et al*. (2006)[13]	Low	Low	Low	Low	Low	Low	Good
Gauri doshi-mehta *et al*. (2012)[14]	Low	Low	Low	Unclear	Unclear	Low	Fair
Abdullah ekizer *et al*. (2016)[15]	Low	Low	Low	Low	Low	Low	Good
Alissa maria varella *et al*. (2018)[16]	Low	Low	Low	Unclear	Low	Low	Fair
Sevin erol üretürk *et al*. (2017)[17]	Low	Low	Low	Unclear	Low	Low	Fair
Dipika mistry *et al*. (2020)[18]	Low	Low	Low	Low	Low	Low	Good

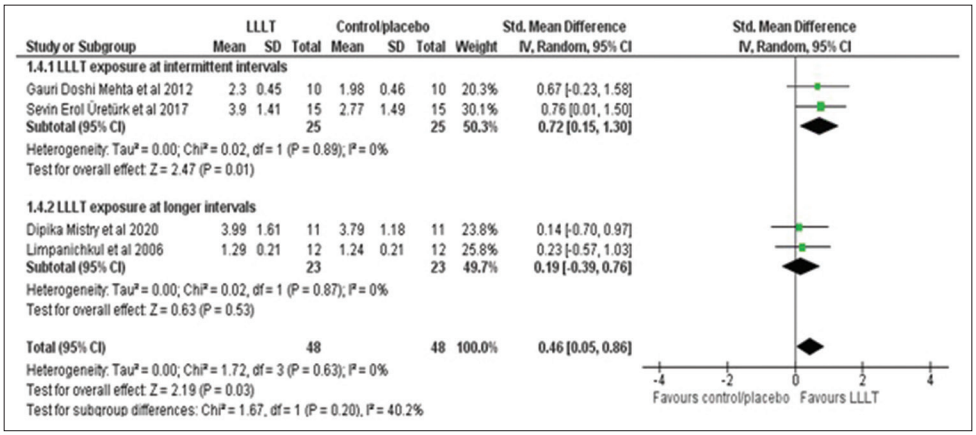

Figure 2: (Meta-analysis) Forest plot of orthodontic tooth movement in intermittent versus long-term interval exposure of LLLT

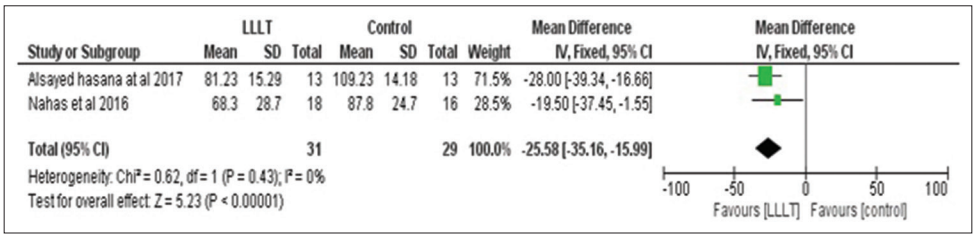

Figure 3: (Meta-analysis) Forest plot of duration of time taken for anterior alignment using LLLT versus controls

As far as number of irradiation points are concerned majority of the studies used 8-10 irradiation points based on a root morphology, which shows that for effective acceleration the delivery of LASER needs to

Table 4: Details of LASER used

Author	Type of laser	Wavelength	Energy density	Power output	Time (sec)/ tooth or point	Points irradiated	Frequency of application (days)
Amer Z. Nahas *et al*. (2017)[9]	LED- Ortho pulse	850 nm	150 J/ cm^2	90 mW/ cm^2	20 min/day	Not mentioned	Daily
Gianluigi Caccianiga *et al*. (2017)[10]	Diode LASER	980 nm	150 J/ cm^2	1 W	50 s/segment Total -150s	Six segments	Daily
Mohammad moaffak a. alsayed hasana *et al*. (2017)[11]	Ga-Al-As semiconductor LASER device	830-nm	2.25-J/ sq.cm	150 mW	15 s (1 min/ toot h)	4	Repeated on days 3, 7, 14, and then every 15 days starting from the second month until the end of the leveling and alignment stage
Irfan Qamruddin *et al*. (2017)[12]	Ga-Al-As diode LASER	940 nm	7.5 J/ cm^2	Not mentioned	Not mentioned	5	Applied at 3-week intervals
Limpanichkul *et al*. (2006)[13]	Ga-Al-As diode LASER	860 nm	25 J/ sq.cm	100 mW	184s	8	First 3 day of each month- for four months
Gauri Doshi-Mehta *et al*. (2012)[14]	Ga-Al-As diode LASER	810 nm	8J/ sq.cm	100 mW	100s	10	0,3,7,14,45,75,105,135
Abdullah Ekizer *et al*. (2016)[15]	OsseoPulse1 LED device	618 nm	20 mW/ cm^2	Not mentioned	20 mins per day	Buccal aspect of teeth	Over a period of 21 successive days (20 minutes per day)
Alissa Maria Varella *et al*. (2018)[16]	Ga-Al-As diode LASER	940 nm	8 J/cm^2	100 mW	10s	10	Repeated for 3 consecutive days at start of canine retraction, 4 weeks later, 8 weeks later. (total period of 12 weeks)
Sevin Erol Üretürk *et al*. (2017)[17]	Ga-Al-As diode LASER	820 nm	5-J/ sq.cm	20 mW	100s	10	0,3,7,14,21,30,33,37,60,63,67,74,81,84,90 days
Dipika Mistry *et al*. (2020)[18]	Ga-Al-As diode LASER	808 nm	1.97 W/ sq.cm	0.20 W	10 seconds per point	8	Every 4 weeks on day 0, 28, 56, and 84; over 12 weeks.

be distributed to many points rather than one. Hence, uniform LASER irradiation from all the sides showed better results than increasing the magnitude of the irradiation. Irradiation intervals also varied in different studies; studies with positive results had almost more than 10 exposure per month, whereas studies with 1-3 exposures failed to give positive results.[21,22]

Four studies were included in quantitative analysis after considering the clinical homogeneity of the studies with respect to their methodology (i.e., wavelength in the range of 800-860 nm, RCT studies which had premolars extracted comparing the rate of canine retraction under LLLT exposure with a control group).[13,14,17,18]

Figure 2 shows a forest plot comparing the standard mean difference in the rate of canine retraction between two subgroups, intermittent frequency/weekly interval of LLLT exposure, and long-term frequency/monthly interval of LLLT exposure.

When comparing the two subgroups, there was a statistical significance of P =0.01 in the rate of tooth movement for the intermittent interval LLLT exposure subgroup which showed Standard Mean Difference (SMD) = 0.72 mm; 95% confidence interval (CI), I^2 = 0% when compared to the monthly/long-term interval LLLT subgroup which showed a less statistical significance in the rate of tooth movement of P =0.53 at SMD = 0.19 mm, 95% CI, I^2 = 0%. [Figure 2]

When considering the total overall effect in the rate of canine retraction, there is a statistically significant increase in the rate of canine retraction which favors intermittent exposure of LLLT (SMD = 0.46 mm; 95% CI; P = 0.03) and level of heterogeneity is low (I^2 = 0%). [Figure 2]

Two studies were selected for quantitative assessment of time duration for alignment [Figure 3][9,11] which shows the forest plot comparing the mean number of days taken for achieving alignment of anterior teeth with and without LASER application. Heterogeneity level was very low and the meta-analysis performed indicated a statistically highly significant reduction in the number of days taken for aligning anterior teeth in the test group (SMD = -25.58 days; 95% CI; P <.00001) and level of heterogeneity is I^2 = 0%.

Discussion

Summary of evidence

Adult patients seeking orthodontic treatment warrant a reduction in duration of fixed mechanotherapy. Acceleration of OTM has been attempted by numerous

methods and the most promising noninvasive is the application of LLLT.[2,3] Several authors have evaluated the effect of LLLT on OTM but there is less clarity on the difference in rate of tooth movement with a varied interval of application of LASER, number of irradiation points necessary to achieve optimal acceleration in tooth movement.[9-18] Hence, the aim of the systematic review was to quantitatively analyze the effect of variation in the frequency of application of LASER on the rate of OTM and analyze the difference in the time taken for alignment of anterior teeth.

Mechanism of bone remodeling brought about by photobiomodulation are listed below[23-25]:

1. LASER light energy increases the metabolic activity and bone turnover by increasing the amount of ATP (Adenosine Triphosphate) in osteogenic cells.
2. Sensitivity of osteoblast and osteoclast to low intensity LASER light is used to augment cell proliferation and function.
3. Fujita *et al*.[25] reported that LLLT increases the rate of tooth movement by enhancing the expression of RANK (receptor activator for nuclear factor kappa) and RANKL (Receptor activator for nuclear factor kappa ligand).

Systematic data search yielded two RCTs that had studied the duration taken for alignment of lower anterior teeth with and without the application of low-level LASER in patients who did not require premolar extraction for orthodontic alignment.[9,10] Both the studies reported a statistically significant reduction in duration required for alignment of teeth in the test group.

Alsayed Hasan *et al*.[11] studied the duration taken for alignment of anterior teeth with and without the application of LLLT.[11] LASER was applied at 1,3,7, and 14 days, followed by application every 15 days till alignment and leveling were completed. They found that there was a 26% reduction in the overall treatment time in the test group when compared to control.

Quantitative evaluation of the duration taken for achieving alignment and leveling was done using data from two studies.[9,11] It was found that there was a highly significant reduction in the number of days required to achieve alignment and leveling in the test group [Figure 3].

LASER irradiation in most of the studies was done on specific regions around the tooth that was intended to move rapidly, called irradiation points. Point irradiation varied for different studies from as low as 4 points to maximum of 10 points. A study by Caccianiga *et al*.[10] divided oral cavity into segments instead of specific points. Studies by Nahas *et al*.[9] and Ekizer *et al*.[15] used light emitting diode device which did not have point irradiation or segments, instead just exposure of light from buccal aspect of the teeth. Irradiation points were specifically used in researches that studied the rate of canine retraction in extraction cases; Üretürk *et al*.[17] chose 10 points in their study, of which five were on buccal and five were on a palatal aspect. Studies with a greater number of irradiation points claimed an increased acceleration of OTM.[11,13,16] By increasing the number of point irradiation with small time interval of 10-15 seconds, adequate LASER energy is delivered to the cells and also reduces the chance of heat damage to surrounding tissues.

Frequency of interval between LASER exposure usually was carried out once in 3-4 weeks in majority of the studies; such exposure is common in patients requiring an increase in rate of tooth movement.[10,11,12,17] After initial leveling and alignment application of LLLT once in 3 weeks showed a considerable decrease in the time period needed for space closure.[10,11,14,17] Research by Nahas *et al*.[9] and Caccianiga *et al*.[10] showed 10 exposures per month in a nonextraction case that had significant changes in accelerated OTM in comparison to study where lesser duration of exposure was present.[15]

Four RCTs qualified for quantitative evaluation of the difference in the rate of OTM when LASER was applied at different time intervals because LASER used was in a narrow range of LASER (800-860 nm). When the frequency of LASER application was compared, two studies have applied LASER in intermittent manner: 0, 3, 7, 14 days, and every 15th day till canine retraction was completed and 0, 3, 7, 14, 21, 30, 33, 37, 60, 63 days, and 67th day.[14,17] Alternatively, LASER was applied every four weeks by Mistry *et al*.[18] and first three days followed by once a month for 4 months by Limpanichkul *et al*.[13]

Meta-analysis was done by subgrouping the studies into intermittent interval and long interval LASER exposure studies to compare their effects with control [Figure 2]. It was found that intermittent exposure to LASER of minimum four applications in the first month produced a statistically significant increase in rate of tooth movement when compared to control (P =0.01), in contrast to the long interval studies in which there was no difference between the two groups (P =0.53) in the rate of canine retraction [Figure 2]. Test for overall effect yielded a statistically significant value of P =.03 which denotes that there is a statistically significant increase in the rate of OTM when LLLT was applied at intermittent intervals than long intervals of once a month.

Doshi-Mehta *et al*.[14] studied the rate of canine retraction in 20 orthodontic patients with application of LASER and they found that there was a statistically significant

increase in the rate of OTM of 56% at the test site when compared to control at the end of 3 months. This positive effect could be due to the low intensity of the LASER used with a power output of 0.25 mW, but as per the result of the meta-analysis performed, it can be inferred that there is a definitive effect due to the variation in the number of applications of LASER in the first month.

When the studies of Limpanichkul *et al*. and Mistry *et al*. were compared, it was found that both the studies used similar energy intensity of LASER but there was a variation in the frequency of application of LASER when compared to Doshi-Mehtha *et al*. and Uretruk *et al*.[13,14,17,18] In the intermittent group, there is minimum application of four times in the first month 0,3,7, and 14 days in the first month and 0,3,7,14,21, and 30 days, respectively.[14,17] In the long interval group, Mistry *et al*. have applied LASER on 0, 28, and 56 days and Limpanichkul *et al*. have applied on the first three days which was repeated in the subsequent months.[13,18] Therefore, it is clear from the results of meta-analysis that there is a definitive positive effect on the rate of OTM when LASER irradiation was given for minimum four applications in the first month.

There is possibly an increased initial impetus to OTM provided by the periodically spaced LASER application in the first month of canine retraction by Doshi-Mehta *et al*. and Uretruk *et al*.[14,17] The biological mechanism behind this initial impetus is an area for future research.

Limitations

Parameters of LASER used like optimal wavelength, energy intensity, effects of change in the number of irradiation points, time spacing between LASER applications, etc., need more clarity and are areas of future research.

Conclusion

LLLT can be suggested as an adjuvant promising procedure with potential to accelerate OTM considering the following points of the study:

1. Meta-analysis shows that frequent application of LLLT for a minimum of four times in the first month of canine retraction produced a statistically significant increase in rate of OTM.
2. There was a statistically significant reduction in the duration taken for alignment of anterior teeth with LLLT.

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Conflicts of interest

There are no conflicts of interest.

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