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REVIEW ARTICLE

Effects of laser therapy on patients who underwent rapid maxillary expansion; a systematic review

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Abstract

Rapid maxillary expansion (RME) is one of the common treatments of transverse maxillary deficiency, and low-level laser therapy (LLLT) is one of the recommended solutions to enhance biological wound or bone healing. This review article aims to answer the following question: "What are the effects of LLLT, on patients who underwent surgical or non-surgical RME, in improving clinical success, wound healing, and bone regeneration?" A search in PubMed, Scopus, Web of Science, and ProQuest databases was performed, with a focus on the appropriate key words. Related articles, up to May 2017, were screened, and the full text of the randomized controlled trials (RCT) were comprehensively read and subjected to quality assessments. A total of 1804 articles were included after the initial search. Four RCTs were eligible in randomization and methodology. The applied wavelength varied from 660 to 830 nm with an output range of 40–100 mW. Also, the highest exposed energy was 420 J/cm^2 and the lowest was 100 J/cm^2. The exposure time differed from 20 to 84 s in each defined point in the palate. Based on the RCTs available, LLLT is better to be used at initial phase of RME, because it has some benefits in increasing the rate of bone remodeling.

Keywords Bone regeneration · Low-level light therapy · Maxilla · Palatal expansion technique

Introduction

Maxillary constriction can lead to several problems such as poor esthetics, occlusal dis-harmony, narrowed pharyngeal airway, increased nasal resistance and mouth breathing, altered tongue posture, and obstructive sleep apnea [1, 2]. In all malocclusions, transverse discrepancy is the most common problem encountered [3]. Three methods are suggested for treating maxillary constriction: non-surgical orthodontic rapid maxillary expansion (RME), surgically assisted rapid palatal expansion (SARPE), and segmental LeFort osteotomy [4, 5]. RME has become more common due to its many positive effects on general health. Also, dental or skeletal transverse maxillary discrepancies can be remarkably treated by this method [6]. Moreover, RME can improve nasal breathing by increasing the nasopharyngeal airway [7]. For problems such as large transverse discrepancies (> 7 mm), narrow intercuspid dimensions, and maxillary arch length deficiency with crowding, the treatment of choice is SARPE [5, 8]. The clinical procedure for maxillary expansion consists of an active phase with induced lateral forces and a passive phase with retainer maintenance [9]. One of the possible encountered obstacles during RME is rapid relapse of treatment (if retainers are not used) [10]. Insufficient bone regeneration in the mid-palatal suture (MPS) is one of the involved causes of relapsed treatments. Therefore, accelerating the bone regeneration in MPS is encouraged by researchers [11].

Low-level laser treatment (LLLT) is a non-invasive treatment that provides low energy outputs and does not increase temperature of the site higher than the natural norms [12]. It provides an inexpensive treatment that can be used in many orthodontic treatments, as it generates an array of transient biochemical factors that result in cascading biological reactions [13]. LLLT has shown promising results in the

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expression of cytokines and promotion of wound healing, angiogenesis, cell proliferation, and bone repair and remodeling, by increasing collagen production [13–17]. The effect of LLLT on bone remodeling is well-tracked by Noda et al., who claimed that healing of the tooth extraction socket was enhanced by high-frequency pulsed low-level diode laser irradiation [16]. Also, more homogenous trabecular configuration can be achieved by LLLT, after alveolar bone repair, as suggested by Romao et al. [17]. In vivo studies mentioned that LLLT is advantageous during MPS expansion, by accelerating the formation of better bone and osteoclast differentiation [14, 15]. A valuable and comprehensive textbook on the role of laser in dental sciences has been recently released [13]. One of its chapters is devoted to elaborating the influence of laser on orthodontic purposes, such as gingivoplasty, impacted tooth exposure and bracket placement, pain reduction and post-op managements, and tooth movement. Nevertheless, the role of LLLT on RME and further bone regeneration success is not mentioned exactly.

Based on what was mentioned above and recent focus on the benefits of LLLT, as a non-invasive method, the aim of the current review study is to answer the following question: "What are the effects of using LLLT on clinical success, wound healing, and bone regeneration, compared to other possible methods, in patients who underwent surgical or non-surgical RME?" The null hypothesis is that LLLT does not have any positive effects on improving results of RME.

Methods

Study design

To enhance the structural reporting of the articles, the reviewing setting was in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline [18].

Initially, a clinical question was defined for screening the qualified clinical studies based on PICO: Patients with constricted maxilla (P, population) who underwent LLLT (I, intervention), compared to other methods (C, comparison), following surgical or non-surgical RME, that caused improvements in clinical success, wound healing, and bone regeneration (O, outcome).

A data search was performed using PubMed, Web of Science, Scopus, and ProQuest electronic databases of articles, based on MeSH and non-MeSH terms in simple or multiple conjunctions (Table 1). The search was conducted manually up to May 2017. Then, the Endnote software version 7 (Thomson Reuters, NY, USA) was used for final confirmation, cross matching, and avoiding any missing of data.

Two independent reviewers (A.D. and M.A.) qualified the eligible articles for review. To select the studies, all obtained reports were reviewed, and titles and abstracts were screened for relevance. The review articles and references from different studies were used to identify the relevant articles. In case of disagreement between reviewers, it was discussed until mutual agreement was reached. Reviewers' agreement was tested with the Cohen κ test using the MedCalc software (MedCalc Software, Ostend, Belgium).

The studies were subjected to modified Jadad Score Calculation for Critical Appraisal, to lower the risk of bias (Table 2) [19]. The full text of relevant abstracts was obtained, and selected using the following inclusion and exclusion criteria.

Inclusion criteria

- Randomized clinical trials (RCTs) and prospective studies that investigated the effect of LLLT on surgical or non-surgical maxillary expansion.
- Clinical research on at least five patients
- Maintaining the standard indications and guidelines of LLLT (like maintaining Helsinki declaration guidelines of clinical trials, using non-toxic chemical agents (if needed), considering non-hazardous energy density during procedure, paying attention to the safety of both the examiners and patients, and preparing follow-up courses after intervention).
- Performing at least one standard test to evaluate the clinical effects or side effects of LLLT

Table 1 Applied PICO keywords

PICO	Key words
Population	(Maxilla [MeSH Term]) or (Malocclusion [MeSH Term]) or (Maxillary Deficiency) or (Maxillary Constriction) or (Cross bite)
Intervention and comparison	(Palatal Expansion Technique [MeSH Terms]) or (Low-Level Light Therapy [MeSH Terms]) or (Laser therapy [MeSH Terms]) or (Lasers [MeSH Terms]) or (Rapid Palatal Expansion) or (Rapid Maxillary Expansion [MeSH Term])
outcome	(Bone Healing) or (Bone Regeneration [MeSH Terms]) or (Bone Remodeling [MeSH Terms]) or (Prodromal Symptoms [MeSH Terms]) or (Signs and Symptoms [MeSH Terms]) OR (Wound Healing [MeSH Terms])

Table 2 The modified Jadad score calculation of selected studies

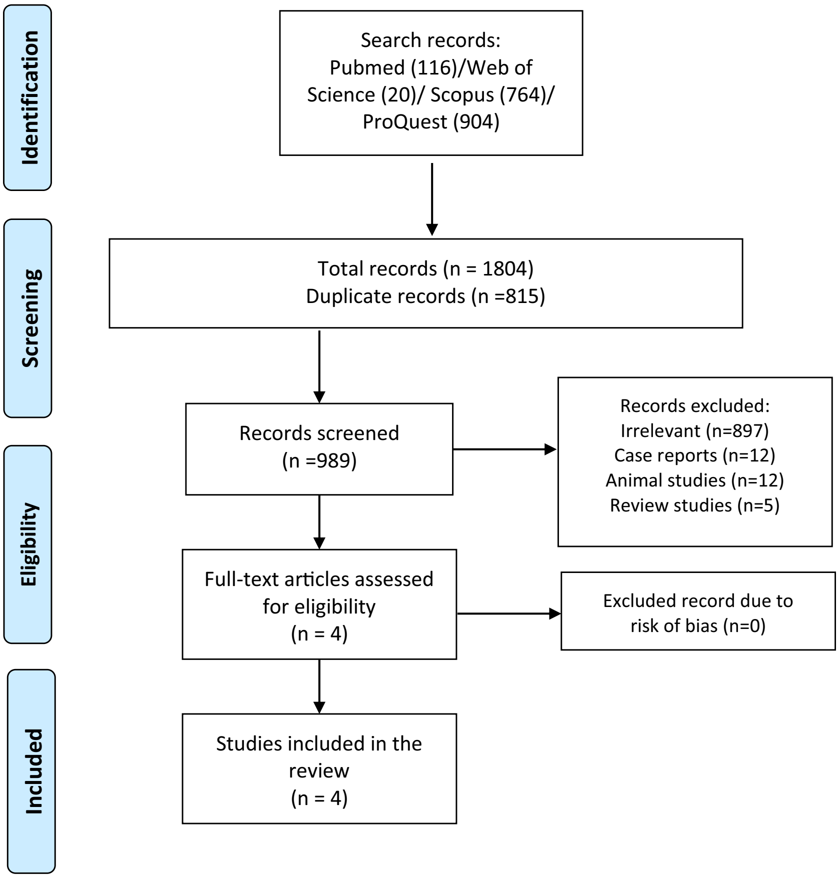
Jadad scale		Cepera et al.	Angeletti et al.	Garcia et al.	Ferreira et al.
Randomization	Was the study described as randomized?	1	1	1	1
	Was the randomization described and appropriate?	0	1	1	1
Blinding	Was the study described as double-blind?	0	0	0	0
	Was the double-blind method appropriate?	0	0	0	0
An account of all patients	Was there a description of withdrawals and dropouts?	1	1	1	1
	Was there a description of the inclusion/exclusion criteria?	1	1	1	1
	Was the method used to assess adverse effects described?	0	0	0	0
	Was the method of statistical analysis described?	1	1	1	1
Result		4	5	5	5
Quality of study		Moderate	Moderate	Moderate	Moderate

Exclusion criteria

- Case reports
- Animal studies
- In vitro studies
- Studies with missing data
- Repeatedly published studies; the last version was included
- Studies in languages other than English
- Studies with Jadad score of < 3 (for eliminating the risk of biases)

The initial literature search yielded 1804 articles (PubMed, $n = 116$/Scopus, $n = 764$/Web of Science, $n = 20$/ProQuest, $n = 904$), of which 989 articles remained after removing the duplicates. After initial screening based on the title and abstract, four studies [20–23] were found eligible to be reviewed (Fig. 1).

Fig. 1 The flowchart of searching strategy based on PRISMA guidelines



Data extraction

The full-text of all articles was reachable for initiating the review process. The following data were collected for each study: author, year, study design, participants (age, gender), diagnosis, details of the administered laser, monitoring tests before and after LLLT, and clinically significant outcomes. After gathering information, the possibility of preparing a meta-analysis was judged by an independent statistician and epidemiologist. As the collected data were vastly heterogeneous, no meta-analysis was prepared.

Results

A total of 1804 articles were included in the study after the initial search, and 989 articles remained after removing the duplicates, of which four studies were eligible to be screened. The full texts of these articles were gathered, and the ones fulfilling the inclusion criteria were taken into account. Relying on the modified Jadad scale (Table 2), three studies with a score of 5 [20, 22, 23] and one with a score of 4 [21] were included for reviewing. None of the studies included were highly potential for risk of bias.

All of the reviewed studies were RCTs on a total of 110 patients, aged ranging from 6 to 33 years (Table 3). Regarding the clinical problem, two studies focused on patients with transverse maxillary deficiency [20, 22], one on Cl I or II malocclusion [23] and one on any kind of RME treatment need [21] (Table 3). One study tried surgical approach alongside RME [20], and the others used non-surgical treatments [21–23].

Regarding the treatment methods (Table 4), all of the studies irradiated the palate at 10 [21], 3 [20], or 4 [22] points around MPS; also, one study irradiated 4 intra-suture and 2 extra-suture points in one of their study groups [23]. All studies used the diode laser for irradiation with the applied wavelength varying from 660 to 830 nm, and output range of 40–100 mW. The highest applied energy on the palatal mucosa was 420 J/cm^2 [20], and the lowest was 100 J/cm^2 [21].

The exposure time was different amongst the studies; Angeletti et al. irradiated LLLT for 84 s in each point (3 points overall, 3 × 84 = 252 s) [20], Garcia et al. used LLLT for 60 s in the intra-suture points (4 × 60 = 240 s) and 30 s in the extra-suture points (2 × 30 = 60 s) [23], and Ferreira et al. used LLLT for 20 s per defined point (4 × 20 = 80 s) [22].

The rate of RME was different amongst the included studies. Two of them administered one full turn screw opening after installation and two half turns daily, until achieving overcorrection [21, 22]. One of them activated the screw a quarter turn (0.20 mm), twice a day, until achieving 50% transversal overcorrection [23], and the last one opened the screw 1.6 mm inter-operatively and twice a day after 4 days' latency [20]. Cepera et al. found improved MPS opening and accelerated bone regeneration [21]. Angeletti et al. stated that bone regeneration after LLLT following the SARPE approach caused significant mineralization [20]. Both Garcia et al. [23] and Ferreira et al. [22] indicated that LLLT resulted in a better healing process following RME.

Discussion

The data regarding the clinical success of LLLT after RME, relative to either the radiation dose or the number of sessions, seemed to lack validation, since most of the released articles are animal studies [24, 25]. Therefore, the present study tried to comprehensively review valuable clinical studies on this scope.

LLLT has provided several positive impacts on orthodontic science, such as analgesic effects during the orthodontic maintenance phase, better healing of scars caused by orthodontic

Table 3 Details of reviewed articles

Author	Study design	Objectives	Number of gender of patients	Age range (mean), years	Treatment plan	Diagnosis
Cepera et al.	RCT	Effect of LLLT on bone regeneration after RME	27	8.2–12.1 (10.2)	RME by Hyrax expander	Any kinds of RME treatment need
Angeletti et al.	RCT	Effect of LLLT (GaAlAs) on bone regeneration in mid-palatal anterior suture after surgically assisted RME	30	18–33	Surgically assisted RME by Hyrax expander	Maxillary transvers deficiency
Garcia et al.	Single-blind RCT	Clinical effect of LLLT after RME	39	6–12 (8.45)	RME by Hyrax expander	Cl l or Cl ll malocclusion
Ferreira et al.	Single-blind RCT	Effects of LLLT on bone regeneration of the mid-palatal suture after RME	14	8–14 (11)	RME by Hyrax expander	Transverse maxillary deficiency

Table 4 The study grouping, clinical tests, and clinical significant results of reviewed articles. Significant (Sig), difference (Dif), mid-palatal suture (MPS), optical density (OD), rapid maxillary expansion (RME), low-level laser therapy (LLLT)

Author	Types of treatments	Irradiant	Wavelength	Power	Energy/ energy density	Irradiated points	Exposure duration	Time of exposure/application	Screw opening	Measurement tool	Outcomes
Cepera et al.	Group 1: laser application at 10 points around MPS	Diode laser	780 nm	40 mW	10 J/cm^2 per point	10 points: 4 anterior to Hyrax screw, 2 lateral, 4 posterior to screw	10 s	Stage1: (days 1–5 of activation) Stage 2: (at screw locking, on 3 consecutive days) Stages 3,4, and 5: 7, 14, and 21 days after stage 2	1 full turn on the first day and a half turn daily until achieving overcorrection	OD of occlusal radiographs at following time points: T1: Initial T2: Immediately after initiating expansion T3: 3–5 days after T2 T4: 30 days after T3 T5: 60 days after T4	-Sig dif between T3 and T2, T2 and T2, T5 and T4 ($P < 0.05$). -There was no sig dif in OD of two groups in T1 or T2, in contrast to following time points: T3 ($P < 0.008$), and T4 (0.006). -Sig decrease in laser group in OD from T1 to T2, increase from T4 to T5 and T2 to T5 ($P < 0.001$). But in control group, there was no sig dif in OD between stages. -In conclusion, LLLT improved the opening of the MPS and accelerated the bone regeneration process
	Group 2: control	–	–	–	–	–	–	–			
Angeletti et al.	Group 1: laser application at 3 points on anterior MPS	GaAlAs diode laser	830 nm	100 mW	140 J/cm^2 per point	3 following points: A: incisive papilla B: 2 mm right of MPS C: 2 mm left of MPS	84 s	8 sessions: 24 h after surgery and the subsequent sessions at a regular intervals of 48 h	Activated intraoperatively for 1.6 mm. Opening twice a day after 4-day latency	OD of periapical digital radiographs at: F0: pre-operation F1: 30 days post-operation F2: 60 days post-operation F3: 90 days post-operation F4: 120 days post-operation F5: 210 days post-operation	-Results of F0 were significantly greater than F1, F2, F3, F4, and F5 ($P < .001$). -Laser group had sig higher bone regeneration than control ($P < .001$) -After 7 months, ossification of MPS was not completed. -In conclusion, bone regeneration associated with the use of LLLT after SARME was remarkably with higher mineralization rates in the laser group
	Group 2: control	–	–	–	–	–	–	–			
Garcia et al.	Group 1: laser application at 4 intra-suture points and 2 extra-suture points	InGaAlP laser	660 nm	100 mW/cm2	332 mW/cm^2 per point	6 points: A: intra-suture points (1 vestibular and 3 palatal) B: extra-suture points (2 palatal)	A: 60 s B: 30 s	7 applications on days 1, 7, 14, 28, 42, 56, and 70; all during the retention phase of RME	Activated quarter turn (0.20 mm) two times a day until 50% transversal overcorrection	Optical density of prepared CBCT after last activation (CBCT1), and 75 days later (CBCT2)	-Intra-suture distance in CBCT1: No sig dif in the expansion, but slightly greater in laser group

Table 4 (continued)

Author	Types of treatments	Irradiant	Wavelength	Power	Energy/ energy density	Irradiated points	Exposure duration	Time of exposure/application	Screw opening	Measurement tool	Outcomes
	Group 2: control	–	–	–	–	–	–	–			-Intra-suture distance in CBCT2: sig dif in superior distance ($P = 0.040$), and sig decrease of well-defined margins of MPS. -Sig dif in approximation of anterior superior suture ($P = 0.008$) and of posterior superior suture ($P = 0.001$) in laser group. -In conclusion, LLLT appears to stimulate the repair process during the retention phase after RME
Ferreira et al.	Group 1: laser application at 4 point around MPS	GaAlAs diode laser	780 nm	70 mW	35 J/cm^2 per point	4 points: Incisal papilla; right and left to raphe; most posterior region along MPS and front of Hyrax screw	20 s	12 sessions: twice a week in the first month, and once a week in the second month	One full turn after installation and two half turns daily until achieving overcorrection	OD of CBCT on: T0: initial phase T1: final phase	-Sig dif between T0 and T1 in OD of experimental groups ($P = 0.00$). -Final OD (T1) was significantly different between laser and control groups ($P = 0.005$). -In conclusion, LLLT had a positive influence on bone regeneration of the MPS by accelerating the repair process.
	Group 2: control	–	–	–	–	–	–	–			

appliances, and accelerating bone repair [13, 15, 26–28]. An in vitro study on biostimulatory effect of LLLT on human osteoblasts showed rapid increase in vascular endothelial growth factor [27]. Also, another study observed an increase in proliferation and phenotypic expression of osteoblast cells (derived from MPS) after LLLT [29]. During the progressive stages of wound stabilization and healing, many cellular and biochemical pathways are potential recipients being activated by low-level laser photonic energy at wavelengths between 600 and 1400 nm [13].

Relying on gathered information from the current review study, the null hypothesis was rejected, since LLLT improved both wound healing and bone regeneration of MPS during and after RME.

Most included studies were on children, except for one study which included youths (18–33 years old) [20]. In adult patients, the MPS is much more mature, with higher integration and interdigitating, so RME is more susceptible to failure; therefore, a surgical-associated approach with RME is required [30]. Angeletti et al. [20] observed the effects of LLLT on bone regeneration in the mid-palatal anterior suture after surgically assisted RME. They used GaAlAs laser (power = 100 mW, wavelength = 830 nm) in eight treatment sessions, with 48-h intervals, on 3 points in MPS (energy density per point = 140 J/cm^2). The reason of using GaAlAs laser was based on released animal studies that showed this laser device increased fibroblast proliferation and the amount of osteoid formation during RME [15, 31]. They used digital radiographs (occlusal and periapical) for measuring optical density (OD) of the bone. Although, these radiographs are acceptable for observation [31], cone beam computed tomography (CBCT) seems to be more appropriate. By CBCT, superposition of tissues can be avoided, and the density is more stable and reliable [3]. Back to Angeletti et al.'s study, they claimed that LLLT caused significant increase in bone regeneration after surgically assisted RME.

Ferriera et al. observed the effect of LLLT on bone regeneration of MPS after RME with the aid of CBCT [22]. They administered the Hyrax expander appliance that was activated one full turn after installation, and two half turns daily. All reviewed studies used this expander appliance, as it facilitates LLLT, by not having any acrylic base on the palatal mucosa that interferes with the irradiation process. Ferriera et al. applied LLLT (power = 70 mW, wavelength = 780 nm) with 35 J/cm^2 dose on 4 points of the MPS, twice a week in the first month, and once a week in the second month (total applied dose = 140 J/cm^2). After 12 sessions of LLLT, the bone regeneration of MPS was evaluated by measuring OD of the prepared CBCT. They scheduled a 4-month retention period, which is in the appropriate range required for new bone formation (3–6 months) [32]. In summary, their final results showed significant improvement in bone regeneration of MPS.

In another study, conducted by Cepera et al. [21], the role of LLLT on bone regeneration of MPS was evaluated after RME. The expansion protocol was one full turn screw opening on the first day, and a half turn daily. The applied LLLT device was adjusted on 780-nm wavelength and 40-mW power (similar to Ferriera et al. [22]), with 10 J/cm^2 density, at 10 points located around the MPS. The LLLT sessions were defined as follows: stage 1: days 1–5 of activation; stage 2: at screw locking, on 3 consecutive days; stage 3, 4, and 5: 7, 14, and 21 days after stage 2. The retention phase was 90 days in this study (about 3 months). They used occlusal radiographs for measuring the OD, and the analyzed data showed that LLLT improved opening of the MPS and the bone regeneration process [21]. The interpretation of OD at different stages of LLLT revealed that: during stage 1 to 2, OD of the LLLT group was significantly lower than the control group, which suggests facilitation in opening the MPS. This result was consistent with Sasaki et al.'s study who claimed that laser accelerates opening of the suture [33]. Also, another animal study showed that LLLT has a paramount role in bone regeneration of MPS, especially in the initial phase that can accelerate suture opening [15]. LLLT may stimulate the osteoblast cells and lead to reduced unwanted buccal orthodontic movements of the supporting tooth [34]. During stages 2–3 and 3–4, no significant differences were found between the test group and controls. During the last phase of the experiment, stages 4–5, higher OD was found in the laser-treated group, meaning higher level of bone regeneration [21].

Garcia et al. observed the influence of LLLT on the repair of MPS after RME [23]. They applied LLLT with 660-nm wavelength, 100 -W power, and 332-mW/cm^2 energy [23] that were different from previous studies [21, 22]. They irradiated 4 points along the MPS for 60 s and each side of the suture for 30 s [23]. Also, seven LLLT sessions were scheduled on days 1, 7, 14, 28, 42, 56, and 70 of the retention phase. They traced CBCT radiographs for measuring OD of MPS [23]. Their quantitative measurements seemed to be more precise than the previously mentioned studies [21, 22]. They measured the following distances: anterior-inferior suture distance, posterior-superior suture distance, and anterior nasal spine suture distance. After separation of MPS, bone resorption, bone regeneration, and fiber rearrangement continue to regain architectural equilibrium [35, 36]. They applied 660-nm wavelength, instead of 780 nm, as Sasaki et al. showed this wavelength can promote mitochondrial enzymes and accelerates tissue repair [33]. However, our reviewer's search on recently published studies lead to controversial results, as some studies believed 810- [36] or 830-nm [37] wavelengths are more effective in both wound healing and bone regeneration, since they are in the absorption spectrum of cytochrome c oxidase (the candidate mitochondrial chromophore in LLLT) [37]. Garcia et al. [23] did not apply LLLT during the activation phase of expansion, as the patients were younger than

Cepera et al.'s study [21], and it was more convenient to irradiate only during the retention phase (seven times in 75 days), similar to Angeletti et al.'s study [20], with eight times irradiation during a retention phase of 39 days. Garcia et al. irradiated the anterior side of MPS more, because the separation seemed to be greater in the triangular-shaped front area, with a wider base at the front portion of the jaw [38]. Nevertheless, a recent systematic review concluded that the available data on MPS opening are not decisive, and it can be parallel or triangular [39]. In summary, their final results revealed that the LLLT group showed more approximation of bone zones in the anterior, posterior, and superior suture with less approximation in the posterior superior suture, than the control group after 75 days.

Conclusion

One of the most important limitations of this was heterogeneity of the included studies, as one was in post-treatment retention, one on young adults as opposed to another on children. Also, there was no consistency of wavelengths, frequency, and mode of application or dosimetry. Although most of the studies on this scope are largely inferential on in vitro and animal studies, the following statements may be concluded at this level of evidences provided by the four RCTs mentioned:

- LLLT is better to be administered at the initial phase of mid-palatal expansion, if it is applicable, because it has some benefits in increasing the rate of bone remodeling.
- The wavelength and power of the irradiated laser was different amongst the included studies, but 780 nm was used in two of them.
- The irradiation points differed amongst reviewed studies, but all of them applied LLLT along the MPS in at least 3 or 4 points.
- LLLT may also have some benefits in increasing the rate of bone deposition in RME; however, more studies are required to make a determinant decision.

Finally, LLLT may be helpful for RME, since it has no side effects, is financially affordable, and requires a short application time. Nevertheless, applying other wavelengths, power, and energy of LLLT, and surveying other biological responses (like pain and edema) and biological factors, are recommended for future investigations. Also, it would be more desirable to use CBCT instead of conventional radiographs for measurements, as it provides better results.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study followed the PRISMA guideline, and no ethical approval was required.

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