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The Effect of Photobiomodulation on Distraction Osteogenesis

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Abstract

Distraction osteogenesis (DO) is a surgical procedure to increase bone height in different body parts. DO includes a surgical incision, wherein the bone is cut and a device is installed for further separation of the two ends by gradual unscrewing of the device screw. New bone gradually forms and fills the gap, and the bone height increases as such.

Photobiomodulation (PBM) or low-level laser therapy (LLLT) enhances the formation of soft and hard tissue such as bone and can, therefore, accelerate the process of DO and shorten the duration of different surgical phases of DO such as latency, activation, and consolidation.

Different laser types with variable exposure settings and protocols have been used for this purpose. The gallium-aluminum-arsenide (GaAlAs) diode laser is the most commonly used laser type for LLLT. This study reviews 18 published articles on the effects of LLLT on DO and summarizes their findings to further elucidate this topic.

Keywords: Photobiomodulation; Low-Level Laser Therapy; Distraction Osteogenesis; Bone Healing; Surgically-Assisted Rapid Palatal Expansion.

Introduction

Photobiomodulation (PBM) or low-level laser therapy (LLLT) is a none-invasive modality extensively used in medicine and contemporary dentistry.[1] It uses a low-level laser (LLL) with a wavelength of 632 to 1064 nm (red and infrared spectra) to stimulate a biological response.[1] PBM increases angiogenesis and cell proliferation by providing adenosine triphosphate.[2-4] The evaluation of the effect of biomodulation by the gallium-aluminum-arsenide (GaAlAs) diode laser on osteoblastic cells reveals that PBM can change the mitochondrial activity of osteoblasts and osteoblastic cell populations in cell culture media.[5]

The effect of PBM on osteoclast genesis and especially on the expression of receptor activator of nuclear factor kappa-B (RANK), receptor activator of nuclear factor kappa-B ligand (RANKL) and osteoprotegerin (OPG) during orthodontic tooth movement has been previously studied.[6] RANKL is a cytokine that belongs to the family of tumor necrosis factors and is essential for the induction of osteoclastogenesis. RANKL bonds to the specific RANK receptor on the surface of osteoclast progenitor cells. On the other hand, OPG inhibits osteoclastogenesis by impairing the bonding of RANK to RANKL. A previous study indicated that the enhancement of orthodontic tooth movement by LLL might be due to the expression of RANK/RANKL while OPG-positive cells were not significantly different between the two groups of laser therapy and no laser irradiation.[6]

It has been shown that PBM accelerates the healing time following oral and maxillofacial surgeries, although the evidence in this respect is still inconclusive.[7] It has been shown that PBM with the GaAlAs laser in a rat model of femur fracture can enhance bone formation in the primary phases of healing.[8] PBM can decrease pain due to temporomandibular joint disorders and help in relieving orofacial pain.[9,10]

PBM has many applications in dentistry, particularly in endodontics, oral and maxillofacial surgeries such as mandibular distraction, oral pathology, and minor intraoral surgeries to accelerate the fixation of mini-screws, in tooth movement enhancement, and in dental prosthesis.[11]

PBM enhances the tissue response, shortens the primary inflammatory response and accelerates the formation of the new bony matrix in bone healing and bone regeneration around dental implants. It enables the formation of a functional bond between the implant and the bone within 8 weeks.[12,13]

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PBM increases the rate of angiogenesis in rats by 3.1 folds. It also enhances the healing of oral ulcers, accelerates the proliferation of fibroblasts and increases the amount of elastic and collagen fibers above their normal threshold in primary stages of wound healing.[14-17] PBM also affects the mitochondria, release of nitric oxide, reactive oxygen species and gene transcription and expression.[18]

In orthodontics, it has been demonstrated that PBM is effective for biomodulation. It also has analgesic effects and stimulates tissue healing.[19,20] Such stimulatory effects are due to the ability of LLL to enhance metabolic changes.[21] PBM is a non-invasive painless modality with no systemic effect. It is easy to perform and does not require expensive equipment.[22] Moreover, a study showed that laser irradiation in a pulse mode had a stimulatory effect on bone formation and cell proliferation, especially osteoblasts in primary phases and cell differentiation.[23]

Ilizarov, a Russian physician, was the first person who introduced distraction osteogenesis (DO) in 1951.[24] DO refers to bone formation between bony surfaces by gradual traction. It is often performed via an incomplete osteotomy or corticotomy and is fixed with an external device. After 5 days of latency, the device is activated at a rate of 1 mm daily (four times of unscrewing per day, each time for 0.25 mm). Next, the consolidation phase starts with the presence of the device at the site to achieve optimal bone strength.[25]

Evidence shows that many pro-inflammatory factors such as bone morphogenetic proteins, interleukins 1, 2, 4 and 6 and RANKL/OPG play a role in different phases of DO, including the consolidation, active distraction and latency phases.[26] It has been proposed that viable tissue under mild but uniform tension induces the mechanotransduction mechanism and stimulates the cell function.[24] Also, evidence shows that new bone (both cancellous and cortical) starts to form radially within 14 days following the initiation of the distraction phase.[27] DO is performed in patients with craniofacial syndromes and disorders, especially children with such conditions by using intra-oral devices.[28-30] DO of the mandible has shown successful results for the resolution of upper airway obstruction in children.[31] The advantages of DO include (I) greater bone movement, (II) not requiring bone grafting, (III) concomitant soft tissue adaptation, (IV) suitability for growing and non-growing individuals, (V) shorter surgical time, and (VI) the ability for more extensive applications.[32]

Adult patients with significant horizontal problems of the base of the maxilla are good candidates for surgically-assisted rapid palatal expansion (SARPE),[33] which is a type of DO and indirectly expands the maxilla.[34] DO of the zygoma and skull is also feasible. DO can be combined with other routine surgical procedures of the jaws as well.[35]

To the best of the present authors' knowledge, no review study is available on the effects of PBM on DO. Thus, this study aimed to review the published articles on the effects of PBM or LLLT on DO.

Materials and Methods

An electronic search of the literature was carried out in Google Scholar, PubMed and Science Direct for English articles with no time limitation, which yielded 21 articles in Google Scholar, 24 articles in PubMed and 38 articles in Science Direct using the keywords "low-level laser therapy AND Distraction Osteogenesis OR surgically assisted rapid palatal expansion". After reading the titles and abstracts, 18 articles were chosen for the evaluation of their full texts. Table 1 summarizes the findings of these 18 articles based on their publication year, title, study design (clinical or experimental), laser type, laser properties, DO protocol, method of bone assessment and final conclusion.

Results

Eighteen articles met the inclusion criteria. These articles evaluated the effect of PBM or LLLT with different types of lasers, wavelengths, power and irradiation protocols on DO and SARPE in different phases of DO. A total of 15 animal studies and 3 human studies were evaluated. Of 3 human studies, 2 studies assessed the effect of LLLT on DO and the remaining one assessed the effect of LLLT on SARPE.

Only one study evaluated the effect of the Ga-As laser with a 970 nm wavelength on DO.[36] Only one study assessed the effect of the Ga-As laser with a 905 nm wavelength on DO.[37] Twelve studies assessed the effect of the Ga-Al-As laser with 808 to 830 nm wavelengths on DO in different areas of the maxillofacial region.

Three studies did not mention the type of the laser and one study only mentioned the commercial brand-name of the laser device.[38]

Discussion

Santinoni et al, in 2017, evaluated the efficacy of LLLT in the healing of maxillofacial bone defects.[54] They only reviewed randomized clinical trials in their systematic review. Studies on transverse maxillary expansion and maxillary cystic defects, one study on DO of the mandible,[37] and studies on cases after tooth-extraction, orthodontic tooth movement and periodontal defects were reviewed. According to their results, PBM can probably enhance the healing of post-surgical defects in the maxillofacial region. The current study reviewed the effects of PBM on DO. Both animal and human studies were reviewed in our study. Another difference between our study and that of Santinoni et al was that we reviewed the applications of PBM not only to the healing phase of defects, but also to the latency and activation phases. Our findings were close to those of Santinoni et al, and the majority of reviewed studies pointed to the stimulatory effect of LLLT on bone healing. Since histological assessment of viable human tissues is not possible in clinical studies, none of the studies

Table 1. Studies Using Different Lasers on DO

Author/Year	Type of Study	Mode of Laser	Laser Properties	DO Protocol	Method of Assessment	Conclusion
Taha et al/ 2018[36]	Experimental (30 dogs)	GaAr	WL=970 nm, Power=2 W, Total Energy=840 J, Duration=420 s	Latency=7 days, Activation=10 days 1mm/d Consolidation=2- and 4- and 8-weeks	Histologic specimens and histomorphometric analysis (photomicrography + morphometric analysis)	LLLT had a positive role as a potential bio-stimulator and local inducer in enhancing bone formation during DO.
Gurler et al/ 2018[39]	Experimental (20 female New Zealand white rabbits)	GaAlAs	Power=150 mW, Energy Density=36 J/cm^2	Latency=5 days, Activation=5 days 1mm/d, Consolidation=15 and 30 days	Histopathological investigation and histological analysis	The use of LLLT in activation period of DO stimulates bone repair.
Freddo et al/ 2016[40]	Experimental (18 female New Zealand rabbits)	GaAlAs	Power=20 mW, Energy Density=20 J/cm^2	Latency=3 days, Activation=7 days 1mm/d, Consolidation=20 days	Picrosirius-stained sections for assessment of collagen fibers/ microscope-coupled camera for assessment of AgNORs	The LLLT-treated group exhibited the greatest bone formation with substantial vascularization.
Medeiros et al/2015[41]	Experimental (24 male New Zealand rabbits)	Not mentioned	WL=808 nm, Power=100 mW, Energy Density=6 J/cm^2	Latency=2 days Activation=10 days 1mm/d	Histomorphometric and histological analysis	This study concluded that bone healing is accelerated with the application of laser irradiation.
Cakir-Ozkan/ 2015[42]	Human study (9 patients with transverse mandibular deficiency of more than 5 mm, 6 males,3 females, mean age: 14.9 years)	GaAlAs	WL=830 nm, Power=40 mW, Energy Density=8.4 J/cm^2	Latency=5 days, Activation= 1 mm/d	CT-scans for bone density and stereological analysis for volume assessment	The retention period can be shortened and mineralization may be increased by using LLLT in mandibular DO.
Abd-Elaal/ 2015[37]	Human study (10 patients:7 females, 3 males, mean age: 31±5.1 years)	GaAs	WL=905 nm, Power=500 mW, Energy Density=20 J/cm^2	Latency=5 days, Activation=7-14 days 1 mm/d, Consolidation=30 days, *Laser was applied during the consolidation period.	Panoramic radiographs using a bone healing score based on the optical density	The use of LLLT on distracted bone was found to increase the quality and quantity of bone and to shorten the consolidation period.
Fazilat/ 2014[43]	Experimental (18 male New Zealand rabbits)	GaAlAs	WL= 810 nm; power=200 mW, irradiation mode= continuous wave energy density= 3 J/cm^2 time=7.5 s	Latency= 5 days, Activation=10 days,0.5 mm/day, Consolidation= 10,20 and 40 days, *laser was applied during latency and activation phases	Macroscopic analysis/ scanning electron microscopeanalysis/ histological analysis	LLLT can stimulate new bone formation only in the early stages of the consolidation period, and has no significant effects on later stages.
Nascimento/ 2013[44]	Experimental (24 male New Zealand rabbits)	Not mentioned	WL= 808 nm, Power= 100 mW, Continous light Density= 6 J/cm^2	Latency=2 days, Activation=10 days, 1 mm/day, Consolidation=not mentioned	Cone-beam computed tomography for bone mineral density analysis	The results suggested an acceleration of bone mineral density after laser and ultrasound irradiation.
Kan/2013[45]	Experimental (16 female New Zealand rabbits)	GaAlAs	WL= 808, Power= 0.25 W, 5 s each point, 6 mm spot size, 7.5 J energy daily	Latency= 6 days Activation=8 days 1 mm/day Consolidation=28 and 56 days	Micro-tomographic analysis for volumetric analysis/plain radiographic analysis for bone density analysis/histology and histomorphology analysis	LLLT in distraction period activates healing of bone and it may decrease the DO period.

Table 1. Continued

Author/Year	Type of Study	Mode of Laser	Laser Properties	DO Protocol	Method of Assessment	Conclusion
Kocyigit/ 2013[46]	Experimental (15 New Zealand rabbits)	Not mentioned	WL= 650 nm, Power= 25 mW, Continuous wave 0.026 W/cm^2, duration=600 s, density= 16 J/cm^2 a day;	Latency= 7 days Activation= not mentioned 1 mm/day Consolidation=43 days	Radiologic evaluation for dual energy x-ray absorptiometry measurement	LLLT and LIPUS are both safe, noninvasive procedures that may improve the outcome of DO treatment, but are both difficult and costly.
Mayer/ 2012[47]	Experimental (24 male New Zealand white rabbits)	AlGaAs	WL= 830 nm, Density= 4 J/cm^2, Power= 40 mW, continuous wave duration=101 s	Latency= 3 days Activation=7 days 0.8 mm/day Consolidation=10 days *laser was applied during activation phase	Histological and histomorphometric analysis	LLLT performed during the activation period has a positive effect on the tissue repair process in a rabbit model of DO of the mandible.
Freddo et al/ 2012[48]	Experimental (5 female Corriedale sheep)	GaAlAs	WL= 830 nm, Power= 50 mW, Energy Density= 120 J/cm^2, Duration=1.41 min	Latency= 5 days Activation=15 days 1 mm/d Consolidation= 13 to 30 days	Computed tomography images for maximal projection reconstruction	LLLT provided increased benefits when applied during the bone consolidation period.
Vannucci/ 2011[38]	Experimental (12 male New Zealand rabbits)	Not Mentioned (manufacturer: Thera Laser)	WL= 830 nm, Power= 40 mW, Continuous emission Density= 10 J/cm^2	Latency= 3 days Activation=10 days 0.7 mm/day Consolidation= 10 days	Histological and histomorphometric analysis/computed tomography analysis/instrumental hardness test/ spectroscopy x-ray fluorescence/x-ray diffraction spectrometry	The results of this preliminary pilot study encouraged the use of LLLT during the healing period.
Krisner et al/ 2010[49]	Experimental (10 male New Zealand rabbits)	GaAlAs	WL= 830 nm, Power= 40 mW, Energy Density= 10 J/cm^2	Latency= 3 days Activation=7 days 0.7 mm/d Consolidation=10 days	Histological analysis	The results suggested that LLLT had a positive effect on the percentage of newly formed bone.
Angeletti/ 2010[50]	Human study (13 patients with maxillary transverse deficiency, age: 18 to 33 years)	GaAlAs	WL= 830 nm, Power +100 mW, Density= 420 J/cm^2, Duration=48 s	Latency= 4 days, Activation= varies depending on treatment goals, 0.4 mm/day, Consolidation=4 months	Digital periapical radiographs for evaluation of optical density as the index of bone regeneration	LLLT accelerated bone regeneration after surgically assisted rapid palatal expansion.
Hübler/ 2009[51]	Experimental (5 male New Zealand rabbits)	GaAlAs	WL= 830 nm, Power= 40 mW, Density= 50 J/cm^2	Latency= 3 days Activation=7 days, 0.7 mm/day, Consolidation=10 days, *laser was applied during consolidation phase	X-ray fluorescence spectroscopy and X-rad diffraction spectroscopy	LLLT had a positive effect on the percentage of newly formed bone, on the chemical composition, and on the crystallinity in the DO sites.
Miloro/ 2007[52]	Experimental (9 New Zealand white rabbits)	GaAlAs	WL= 820 nm, Power= 400 mW, Energy= 6 J	Latency= 1 day, Activation=10 days, 1 mm/day, Consolidation=2,4 and 6 weeks, *laser was applied during activation phase	Ex vivo clinical appearance for bone healing score/histological analysis	The use of LLLT during DO of the mandible resulted in a statistically significant accelerated process of normal bone healing.
Cerqueira/ 2007[53]	Experimental (18 sheep)	GaAlAs	WL= 830 nm, Power= 40 nW, Density= 16 J/cm^2	Latency= 4 days, Activation=10 days, 1 mm/day, Consolidation=21 days	Radiographic and histological analysis	The laser has been more favorable when used in the consolidation period, after bone elongation.

Abbreviations: DO, Distraction osteogenesis; LLLT, Low-level laser therapy; WL, Wavelength.

reviewed by Santinoni et al performed a histological analysis of bone. In the present review, however, animal studies were also included, which histologically analyzed bone. Similar to the study by Santinoni et al, we did not have a uniform specific irradiation protocol for LLL in our reviewed studies.

Ebrahimi et al, in 2012, evaluated the effect of LLLT on bone healing.[55] Their study mainly focused on histological aspects and evaluated the effect of LLL mainly on osteoblasts. They did not limit their review to animal or human studies only. The majority of reviewed studies had an in vitro design or had been conducted in vivo on an animal model. They concluded that LLLT can accelerate the rate of bone healing in the extraction sockets, sites of bone fracture and DO in animal models. Our study, similar to that of Ebrahimi et al, did not limit the review to animal or human studies only. Our findings were in agreement with theirs and confirmed the positive effect of PBM on the healing of DO defects.

Noba et al, in 2017, evaluated the effect of lasers on bone healing after oral surgery.[7] They concluded that PBM accelerates bone healing but there is no standard protocol for its use following surgical procedures. However, evidence in this respect is still inconclusive. The current study, similar to that of Noba et al, assessed both human and animal studies. The reviewed studies did not follow the same protocol of DO. This was also the case in the study by Noba et al. Our findings were in line with those of Noba et al.

Davoudi et al, in 2018, evaluated the articles on the effects of laser therapy on patients under rapid maxillary expansion (RME).[56] They reviewed randomized clinical trials, which had performed RME with/without surgery. They reviewed four articles. Only one study evaluated the effect of laser irradiation on SARPE. They showed that LLL can be used in the primary phases of maxillary expansion because it increases the speed of bone remodeling. Since SARPE follows the principles of DO, we also reviewed a study on the effect of PBM on SARPE.[50] The results of that study were somehow in line with those of Davoudi et al, but contrary to the findings of Davoudi et al, the results from that study showed that lasers should be used not only in the primary and active phases of DO, but also in the consolidation phase.

Moreover, the current study reviewed seven articles on the effects of LLLT on the consolidation phase of DO.[36-38,40,46,49,51] Six studies evaluated the effect of LLLT on the activation phase of DO[39,41,44,45,47,52] and three studies evaluated the effect of LLLT on the latency and activation phases of DO.[42,43,50] However, Angeletti et al[50] did not accurately mention these two phases but the timing of laser irradiation was within these two phases. In a study by Freddo et al, one group was subjected to laser irradiation in the latency and activation phases and the other group in the consolidation phase.[48] Cerqueira et al performed laser therapy in the activation phase in one group and in the consolidation phase in another group.[53] It appears that no consensus exists regarding the most suitable phase of DO for laser irradiation.

The reviewed studies had some differences regarding the location of corticotomy incisions in DO. Studies on the mandible of rabbits also had different locations of incision, including distal to the mental foramen and distal to the first molar,[39] between the first premolar and mental foramen,[48] at 1 mm distance from the mesial root of the first molar,[41,44] in the medial and lateral cortices right in front of the first premolar,[43] anterior to the molar teeth and posterior to the mental foramen,[45] 1 cm mesial to the ramus,[46] between the premolar site and mental foramen,[38,47] and body of mandible right behind the mental foramen.[52] Two studies on the mandible of rabbits did not mention the exact location of the incision and they only discussed that an incision was made in such a way that the inferior alveolar nerve was not traumatized.[49,51] One study was conducted on dogs with an incision line between the mandibular second and third premolars. Two studies evaluated sheep: one of them reported an incision line in the internal and external surface of the gonial angle[40] and the other one reported an incision made in the body of mandible right behind the mental foramen.[53]

The incision lines in the 3 reviewed human studies were as follows: It was on the mandible in two studies; one had an incision at the midline of the mandible[42] and the other one had an incision in the body of mandible right in front of the gonial angle.[37] Another study reported that the incision line was on the maxilla under LeFort I surgery and all sutures including the pterygomaxillary suture were opened.[50] No agreement existed among the studies regarding the incision line for DO of the mandible. Studies on animal models used different incision lines.

No consensus existed among the studies regarding the laser protocol or the irradiated site. One study reported intraoral laser irradiation 5 times a day, perpendicular to the buccal surface for 2 minutes and crest area for 3 minutes in the consolidation phase. They also performed extraoral laser irradiation of the inferior border of the mandible for 2 minutes with 320 mm spot size.[36] Another study irradiated three points measuring 1 cm^2 in size in the buccal and 3 points in the lingual for 40 seconds.[39] Another study reported laser irradiation on the first day of the maturation phase and then for another 9 sessions every 48 hours (a total of 10 sessions). The irradiated sites included 4 points around the DO area for 10 seconds.[40] Two studies performed laser therapy every night for 6 minutes for a total of 24 times. They did not report the exact location of irradiated sites.[41,44] Another study irradiated the laser to 2 areas at the mandibular midline. The first area was the alveolar bone between the roots of central incisors and the second area was at the buccal sulcus depth at the midline 5 mm beneath the first irradiated area. In each session, 2 laser doses were administered (one dose for each area).

The first irradiation was performed during the first 24 hours postoperatively and the remaining irradiation was performed every 48 hours. In total, each patient underwent 8 sessions of laser therapy.[42] Another study reported laser irradiation in the consolidation phase at 4 points of the osteotomy site including two lateral points and 2 points in the inferior region of the body of the mandible. Laser therapy was performed for 12 sessions, each session for 2 minutes.[37] Another study performed the first laser irradiation perpendicular to the surgical site from the medial and lateral aspects in two points after surgery. The diameter of the laser irradiated site was 0.8 mm and the irradiation time was 7.5 seconds. Irradiation was performed once a day for 14 days.[43] Another study irradiated three points in the buccal and three points in the lingual (sites of DO), measuring 6 mm in size for 5 seconds for 6 days.[45] Another study irradiated laser to a point measuring 0.95 cm^2 in size twice a day, each time for 300 seconds for a total of 10 days. They did not mention the exact location of the irradiated site.[46] In another study, the laser was directly irradiated to the site of DO in three points along the osteotomy line for 1.41 minutes immediately after surgery and every 48 hours. The total number of irradiation sessions was eight.[40] Another study reported laser irradiation in the consolidation phase every 48 hours until the end of this phase. They did not report the exact location of the irradiated site.[49] Another study reported laser irradiation of three points at the DO site perpendicular to this location for a total of 1.41 seconds after the activation of the device once every 48 hours. The total number of sessions was four.[47] Another study reported direct irradiation of DO site in the consolidation phase every 48 hours.[38]

In another study, 3 points in the palate measuring 0.06 cm^2 were irradiated (I) the first point was at the incisive papilla, (II) the second point was at the line connecting the two lateral incisors 2 mm right to the mid-palatal raphe, and (III) the third point was at the line connecting the two lateral incisors 2 mm left to the mid-palatal raphe. One dose of the laser was irradiated in each session and each patient underwent a total of 8 sessions of laser therapy. The first laser therapy session was held 24 hours after surgery for 84 seconds each time and laser irradiation was then repeated every 48 hours. The researchers reported that the laser tip was at close contact with the irradiation site.[50]

Another study reported laser irradiation every 48 hours in the consolidation phase for 10 days. They did not specify the exact location of irradiation.[51] Another study irradiated six points on the buccal and lingual surfaces (sites of DO) for 10 days.[52] Another study reported direct daily irradiation of the site of DO with the laser through the skin at 4 points along the corticotomy line.[53]

Considering the results of the reviewed studies, the positive effect of PBM on DO site is obvious. However, a standard protocol for laser irradiation does not exist and there is no consensus among the published studies regarding the phase of DO most suitable for PBM.

Ethical Considerations

Not applicable.

Conflict of Interests

The authors declare no conflict of interest.

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