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REVIEW ARTICLE

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PHOTOBIO-MODULATION IN BONE INJURY REPAIR: A SYSTEMATIC REVIEW

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ABSTRACT

Photobiomodulation (BM) is a non-invasive treatment that uses low intensity light for the effects to generate light response and not heat, it can be continuous wave or pulsed light with low density from 0.04 to 50 J/cm², and power output from 1 to 500 mW, not allowing thermal effects. The effects of photobiomodulation (FBM) on bone fracture repair were analyzed through systematic review of randomized clinical trials and experimental studies of bone fractures addressed with photobiomodulation published in Pubmed/MEDLINE, Science Direct, EBSCO, PEDro and Cochrane Library databases. Between 2000 and 2020, as a comparator the active (control) and placebo groups. **Results:** 88 studies were found, 62 studies excluded and 26 included. Final considerations: The studies have shown beneficial effects on bone fractures such as bone healing, pain relief, function, edema and joint mobility in experimental studies in humans and animals, there is no consensus in the literature regarding parameters in terms of potency, time of treatment and wavelength. New studies should be carried out in order to identify the best FBM parameters in osteogenic property, pain and function were evaluated by the VAS - visual analogue scale or by the evaluation score of 0-10, strength by (flexion test (MultiTest1 -i®; Mecmesin) Limited, West Sussex), and joint mobility by (goniometer).

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INTRODUCTION

Fracture non-union occurs in 10 to 20% of patients with fractures, resulting in prolonged disability. Therefore, it is an important clinical concern [1]. Treating this condition is often painful, risky, time-consuming and expensive. Improvement in the fracture process would have great benefits for patients. Decreasing turnaround time to complete function would reduce medical costs and increase quality of life by decreasing pain and increasing mobility, furthermore, speeding up the healing process can prevent long-term disability caused by joint fracture. The fracture healing process is affected by age, osteoporosis (OP) and diabetes mellitus (DM) [2]. Alternative non-invasive methods have been used in tissue regeneration, such as the use of low-level laser therapy (LLLT), currently called

photobiomodulation (FBM) [3]. In the bone repair process, this therapy is known to exert analgesics, anti-inflammatory effects, in addition to accelerating the regeneration process by providing cell proliferation and differentiation [4]. Photobiomodulation (FBM) can be used in several areas of health. These include regenerative medicine (to heal wounds and ulcers), aesthetic medicine (to improve the appearance of scars), dentistry (to speed up healing of implants), physiotherapy (to reduce pain syndromes), orthopedics (for bone healing) and cardiology (as prevention of restenosis after percutaneous coronary intervention). The molecular effects of low-energy laser irradiation on cells are generally described as "photobiostimulation" and "photobiomodulation" [5]. Conventional laser systems for bone formation consist of Helium-Neonium (He-Ne), Aluminum Gallium Arsenide (AsGaAl), and Gallium Arsenide (GaAs) semiconductors and others in a continuous wave, an

interrupted wave or pulsed light. He-Ne laser irradiation, which has a wavelength of 632.8 nm, promotes the proliferation and differentiation of human and animal osteoblasts in vitro, low power light with the AsGaAl laser, which has a length of 830 nm, and AsGa of 904 nm has a positive effect on osteoblast proliferation [6]. In in vivo and in vitro studies, the increase in the number of osteoblasts in groups irradiated with laser therapy (LLLT) can be explained by the fact that laser induces cell proliferation, presenting biostimulating effects on multipotent cells and causing them to differentiate in osteoblasts, which are the classic producers of bone matrix [7]. Low power laser FBM influences the release of several growth factors involved in the formation of epithelial cells, fibroblasts, collagen and vascular proliferation, in addition to accelerating bone matrix synthesis due to increased vascularization and lower inflammatory response, with a significant increase of osteocytes in the irradiated bone [8]. It is a non-invasive treatment that uses low intensity light irradiation so that the effects generated are light response and not heat. The term laser refers to a device of low intensity or low power [9]. The difference between the various types of lasers is given by their wavelength. The shorter the wavelength, the greater its action and penetration power. Lasers can be continuous or pulsed. Its power is expressed in watts (W), ranging from deciwatts to megawatts and the energy is measured in joules per square centimeter (J/cm²), being equal to the power multiplied by the application time [10]. Within certain limitations and provided that the applicable dose (J) is within the therapeutic range, the higher the dose per treatment session, the faster the accumulated energy threshold will be reached and, therefore, the earlier the positive effect of the treatment. Become evident, assuming the treatment is in fact positive [11]. Low-level light therapy refers to the use of light in the near infrared or red region, with wavelengths generally in the range 600 to 700 nm and 780 to 1100 nm, and laser or LEDs typically have an irradiance or density. Of power between 5 mW cm² to 5 mW cm² in depth. This type of irradiation can be a continuous wave or a pulsed light consisting of a beam of relatively low density (0.04 to 50 J cm²), but the output power can vary widely from 1 mW to 500 mW, in order not to allow thermal effects [12].

clinical studies in humans have led to the assumption that the use of FBM is, in general, safe [17].

METHODOLOGY

A this study consists of a systematic review of the literature addressing the effects of FBM in the repair process in bone fractures. In the search for articles, databases (Pubmed, MEDLINE, Science Direct, EBSCO, PEDro and Cochrane Library) were analyzed between 2000 and 2020. Randomized clinical trials and experimental studies in an animal model with bone fractures addressed were included in the review. With photobiomodulation. As a comparator, the studies must contain an active group (control) and a placebo. The primary outcome was the osteogenic property and the secondary outcomes assessed were pain and function assessed by the VAS - visual analogue scale or by the assessment score of 0-10, strength by (flexion test (MultiTest1-i®; Mecmesin) Limited, West Sussex), and joint mobility by (goniometer) and function by an assessment score of 0 to 10. The study period was carried out from September to November 2021.

RESULTS

The initial search had 88 studies in the databases: 21 results in PubMed, 12 Medline, 16 Science Direct, 8 EBSCO, 10 PEDro and 21 Cochrane Library. 62 studies were excluded for not meeting the inclusion criteria. The final selection process consisted of 26 studies included for full analysis and 6 were selected for presentation in Table 1.

DISCUSSION

When the laser is applied in in vivo studies, and in animals, it is not only the osteoblasts that receive the light but also all the surrounding tissue that is irradiated, so the bone stimulus can be a general and

Table 1.

| Author / Year | Type of studies | Interventions | Results |
|--|--|--|---|
| (Poppi et al., 2011) | In vivo studies and in vitro. | Photobiomodulation (FBM). | Researchers still don't understand fully the mechanism and types of studies in vitro, but try to explain the mechanisms of action during bone repair and formation. |
| (Rogers et al., 2012) | Experimental study in animals. | Laser Therapy (LLLT) associated with phosphate of biphasic calcium, biomaterial and fibrin biopolymer. | The results of an experimental study in animals showed that laser therapy (LLLT) associated with calcium phosphate biphasic, biomaterial and biopolymer of fibrin contributed to regeneration bone. |
| (Rubin et al., 2001) | Animal models and patients. | laser therapy (LLLT) and ultrasound low pulse intensity (LIPUS). | There are few studies on the effect of LLLT in fracture healing in people compared to LIPUS, and that there is still insufficient evidence for establish the positive effect of LLLT on human fracture. |
| (Chang et al., 2014) | Experimental study in Humans | laser therapy (LLLT) and ultrasound therapeutic (US). | The study confirmed that the intervention early low-intensity laser and therapeutic ultrasound helps to improve the pain, range of motion, strength of and to reduce functional disability. |
| (Prabhu et al., 2012) (Mokmeli et al., 2009) | Clinical trial randomized double-blind controlled. | Laser Therapy (LLLT). | Laser therapy (LLLT) can decrease the pain during and after fracture surgery bone and which has a positive effect on wound healing and edema. |
| (Aboelsaad et al., 2009) (Kazem et al., 2010) (Bashardoust et al., 2010) | In models experimental. | Low level laser (LLLT). | The results showed tolerance significantly increased maximum of force before fracture in the laser group, in comparison with the control group. |

FBM has biostimulating effects on bone callus formation, increased bone fracture healing and accelerated regeneration in fracture repair [13]. The laser effect depends on the wavelength, beam type, energy density, energy level and exposure time [14]. The initial effects of the interaction between the laser and biological tissue can cause the release of preforming substances, such as histamine, serotonin, bradykinin, and modify normal enzymatic reactions, accelerating or slowing these reactions and promoting an increase in the production of triphosphate synthesis. Adenosine (ATP) [15]. Findings of extracellular matrix proliferation in cell studies are supported by increased bone healing in animal studies. Animal studies are commonly used as an intermediary between cellular studies and clinical studies [16]. Several experimental studies in animals and

complex effect, including changes in different mechanisms. , as mediator release, even though FBM appears to contribute to bone healing, researchers still do not fully understand the mechanism and types of in vitro studies, and try to explain the mechanisms of action during bone repair and formation [18]. Due to the need for a treatment for the recovery of bone tissue when it is affected by critically sized injuries, several techniques and materials are investigated to facilitate and improve regeneration. Therefore, the results of an experimental study in animals showed that laser therapy (LLLT) associated with biphasic calcium phosphate, biomaterial and fibrin biopolymer contributed to bone regeneration [19]. Laser therapy (LLLT) and low-intensity pulsed ultrasound (LIPUS) are able to stimulate the fracture healing process in animal models and patients in most cases. On the other hand, there are great differences in the number of studies of

laser and LIPUS in humans, and that there are few studies on the effect of LLLT on fracture healing in people compared to LIPUS, and that there is still insufficient evidence for establish the positive effect of LLLT on human fracture [20]. The effects of laser therapy (LLLT) versus therapeutic ultrasound (US) on bone fracture were investigated in an experimental study in humans, and different outcome measures were used to assess the effects of treatments on functional pain disability assessed by the assessment score 0-10 on the pain scale, grip strength assessed by the dynamometer and ROM (range of motion) assessed by the goniometer. The study confirmed that early intervention of low-intensity laser and therapeutic ultrasound helps to improve pain, range of motion, grip strength and to reduce functional disability, and experimental results indicated that the treatment provided effective pain relief and improvement in muscle strength and functional capacity of patients [21]. Laser can also cause analgesia by reducing prostaglandin E2, increasing endorphin levels and increasing serotonin excretion, and stimulation of pain receptors. Laser therapy (LLLT) also has a negative effect on pain neurotransmitters and prevents the accumulation of acetylcholine and pain stimulation in the receptors. In a double-blind randomized controlled clinical trial researchers reported that laser therapy (LLLT) can decrease pain during and after bone fracture surgery and that it has a positive effect on wound healing and edema [22,23]. In an evaluation of the effect of low-level laser (LLLT) on healing surgically created tibial fracture defects in experimental models, however, there are few reports on the application of LLLT using AsGaIn (aluminum gallium arsenide) diode laser for bone healing, the results demonstrated significantly increased maximal strength tolerance before fracture in the laser group compared to the control group [24]. This result suggests that LLLT after surgery on bone fractures can improve the biomechanical strength of new bone during the healing process in an experimental animal model [25] and that the increased tolerance of the maximum force that the bone could withstand was measured by the test of flexion (MultiTest1-i®; Mecmesin Limited, West Sussex) for evaluation of its biomechanical properties, and proved that the test is a valid method for the evaluation of biomechanical strength [26]

CONCLUSION

This article showed the effects caused by photobiomodulation (FBM) or low-intensity laser therapy (LLLT) in the repair of fractures and/or bone injuries in both humans and animals. Positive effects related to bone healing, pain relief, function, edema and joint mobility have been demonstrated. The main criticism is in relation to the parameters used, there was no consensus in the literature regarding the wavelength, power, dosage and time for the treatment to become more effective. New studies should be carried out in order to identify the best FBM parameters in terms of osteogenic property, pain, edema, joint mobility and function.

REFERENCES

- AboElsaad NS, Soory M, Gadalla LMA, Ragab LI, Dunne S, Zalata KR and Louca C (2009). Effect of soft laser and bioactive glass on bone regeneration in the treatment of bone defects (an experimental study). *Lasers Med Sci.* v. 24, n. 4, p. 527-33.
- Aighamdi KM, Kumar A. (2011). Low-level laser therapy: a useful technique for enhancing the proliferation of various cultured cells. *Lasers Med Sci.* v. 27, n. 1, p. 237-49.
- Bashardoust Tajali S, Macdermid JC, Houghton P and Grewal R (2010). Effects of low power laser irradiation on bone healing in animals: a meta-analysis. *J Orthop Surg Res.* v. 5, n. 1, p. 1-10.
- Bleek KS, Kwee BJ, et al. (2015). Boon and Bane of Inflammation in Bone Tissue Regeneration and Its Link with Angiogenesis. *Tissue Engineering.* v. 21, n. 4, p. 354-64.
- Chang WD, WU JH, Wang HJ and Jiang JA. (2014). Therapeutic Outcomes of Low-Level Laser Therapy for Closed Bone Fracture in the Human Wrist and Hand. *Photom and laser surg.* v. 32, n. 4, p. 212-218.
- Dallan LAO, Oliveira SA de, (2000). CO2 laser transmyocardial revascularization surgery. *Rev Bras Cir Cardiovasc.* v. 15, no. 2, p. 89-104.
- Dortbudak O, Haas R, Mailath-Pokorny G. (2000). Biostimulation of bone marrow cells with a diode soft laser. *Clin Oral Implants Res.* v. 11, n. 6, p. 540-545.
- Enwemeka CS. (2011). The Relevance of Accurate Comprehensive Treatment Parameters in Photobiomodulation. *Photom Laser Surg.* 29, n. 12, p. 783-784.
- Forslund JM, Archdeacon MT, et al. (2015). The Pathobiology of Diabetes Mellitus in Bone Metabolism, Fracture Healing, and Complications. *The Am J Orthop.* v. 44, n. 10, p.453-457.
- Forte CPF, Matos AP, et al. (2020). Photobiomodulation Therapy Reduces the Inflammatory Process without Inhibiting Bone Deposition in Rats in an Extraction Model. *Photom Laser Surg.* v. 38, n. 11, p. 673-678.
- Huang YY, Sharma SK, Carroll J, Hamblin MR. (2011). Biphasic dose response in low level light therapy – an update. *Dose-Response.* v. 9, n. 4, p. 602-618.
- Ilic S, Leichter S, et al. (2006). Effects of Power Densities, Continuous and Pulse Frequencies, and Number of Sessions of Low-Level Laser Therapy on Intact Rat Brain. *Photom Laser Surg.* v. 24, n. 4, p. 458-466.
- Kazem Shakouri S, Soleimanpour J, Salekzamani Y and Oskuie MR (2010).Effect of low-level laser therapy on the fracture healing process. *Lasers Med Sci.* v. 25, n. 1, p. 73-77.
- Mergoni G, Vescovi P, Belletti S, Uggeri J, Nammour S, Gatti R, et al. (2018). Effects of 915 nm laser irradiation on human osteoblasts: a preliminary in vitro study. *Lasers Med Sci.* v. 33, n. 6, p. 1189-1195.
- Mokmeli S, Khazemikho N, NIROMANESH, Shirin; Vatankhah Z. (2009). The application of low-level laser therapy after cesarean section does not compromise blood prolactin levels and lactation status. *Photo med Laser Surg.* v. 27, n. 3, p. 509-12.
- Nicolau RA, Jorgetti V. (2003). Effect of low-power GaAlAs laser (660 nm) on bone structure and cell activity: an experimental animal study. *Lasers Med Sci.* v. 18, n. 2, p. 89-94.
- Pinheiro ALB, M. M, Marlene Elizabeth; P.h.d, Gerbi. (2006). Photoengineering of Bone Repair Processes. *Photom Laser Surg.* v. 24, n. 2, p. 169-178.
- Poppi RR, Silva AL da, et al. (2011). Evaluation of the osteogenic effect of low-level laser therapy (808 nm and 660 nm) on bone defects induced in the femurs of female rats submitted to ovariectomy. *Lasers Med Sci.* v. 26, n. 4, p. 515-22.
- Prabhu V, Rao SB, Chandra S, Kumar P, Rao L, Guddattu V, et al. (2012). Spectroscopic and histological evaluation of wound healing progression following Low Level Laser Therapy (LLLT). *J Biophotonics.* v. 5, n. 2, p. 168-84.
- Reddy GK. (2004). Photobiological Basis and Clinical Role of Low-Intensity Lasers in Biology and Medicine. *J Clinic Laser Med Surg.* v. 22, n. 2, p. 141-150.
- Rocha JCT. (2004). Laser Therapy, Tissue Healing and Angiogenesis. *RBPS.* v. 17, no. 1, p. 44-48.
- Rogers GF, Greene AK. (2012). Autogenous bone graft: Basic science and clinical implications. *J. Craniofac. Surg.* v. 23, n. 1, p. 323-327.
- Rola P, Dorozko A, Derkacz A. (2014). The Use of Low-Level Energy Laser Radiation in Basic and Clinical Research. *Adv Clin Exp Med.* v. 23, n. 5, p. 835-842.
- Rosso MP de O, Buchaim DV, Kawano N, Furlanette G, Pomini KT, Buchaim RL. (2018). Photobiomodulation Therapy (PBMT) in Peripheral Nerve Regeneration: A Systematic Review. *Bioeng.* v. 5, n. 2, p. 44.
- Rubin C, Bolander M, Ryaby JP, Hadjiargyrou M. (2001). The use of low intensity ultrasound to accelerate the healing of fractures. *J. Bone Jt. Surg. Am.* v. 83, n. 2, p. 259-270.
- Stein A, Benayahu D, et al. (2005). Low-Level Laser Irradiation Promotes Proliferation and Differentiation of Human Osteoblasts in Vitro. *Photom Laser Surg.* v. 23, n. 2, p. 161-166.