

Low Level Laser in Odontostomatology Practice, a Critical Review

Láser de Baja Potencia en la Práctica Odontoestomatológica, una Revisión Bibliográfica

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ABSTRACT: The application of laser as a therapeutic measure in nervous regeneration in dentistry has not been a discussed subject, even though the knowledge about the response of the peripheral nervous system is very important in practice as well as in the recovery of the patient. It has been proposed that low-level laser (LLL) therapy has beneficial effects on tissues; LLL therapy acts as an analgesic, anti-inflammatory, anti-edematous, anti-cellulitic tool, and it stimulates cellular trofism. In the present study, we conducted a meta-analysis of available literature regarding the response of the injured nerve to low-power laser using search engines EBSCO and PUBMED. The literature refers to the stimulant effect of the low-level laser in the neoformation of vessels and to the existing bibliographic evidence to propose that this mechanism is important in nervous regeneration. There is limited bibliographic evidence on the effects of LLL therapy in dentistry.

KEY WORDS: low level laser, laser, odontology, nervous regeneration.

INTRODUCTION

When we speak of regeneration, we refer to the “replacement of damaged or killed tissues by new ones with the same function” (Garrido & Valiente, 1996), limited to the replacement of specialized cells and their stroma, support, and vascularization. This does not imply that the repair is the replacement of injured tissues by proliferation of both specialist and non-specialist tissues surviving within the area. Regeneration will vary with each type of tissue, and replacement of specialized tissues will depend on the extent of the injury.

In the case of nerve cells this process is complex; nerve cells are unable to proliferate if they are neuroglial cells. Therefore, depending on where the damage occurs, the cells may regain their structure and function; hence, if the nerves are injured and sectioned to the axon level in the peripheral nervous system (PNS), where these cells are found, the damage, depending on the severity, will be repaired. The neuronal function restoration occurs through structural and metabolic phenomena known as the axon

reaction (Gartner & Hiatt, 2002). These reactions occur in case of injuries and occur in three regions of the neuron: at the damaged site (local changes), distal to the damaged site (anterograde changes), and at proximal points to the site (retrograde changes).

This is only possible if the damaged ends remain at a close distance; otherwise, regeneration cannot occur; therefore, it is almost essential that, the damaged ends must be sutured through surgery, but this does not ensure regeneration or acceleration of the process; however, the probability of regeneration increases (Menovsky & Beek, 2001; Gigo-Benato *et al.*, 2004). In addition, there are three types of reactions. The local reaction occurs close to the lesion, where the sectioned membrane fuses to cover the open end, preventing the loss of axoplasm. The damaged area infiltrates into the area of macrophages and fibroblasts, which are responsible for the repair and removal of wastes; an inflammation occurs in the area.

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The anterograde reaction is characterized because in the course of a week the terminal axon is hypertrophic and degenerative, proliferating neurilemma cells (Schwann cells) that occupy the synaptic space and also phagocytizing the remnants of the terminal axon. These cells finally form a column enclosed by the original basal lamina of the endoneurium (connective tissue surrounding the peripheral nerves). Finally, retrograde reaction in the proximal portion of the injured axon suffers degeneration followed by the outbreak of a new axon whose growth is targeted at the neurilemma cells.

Some authors differ on the theories of what happens in relation to fibroblasts, neurilemma cells, perineural cells, and their specific roles in the regeneration process. Some mention that only the endoneurium and perineurium fibroblasts are involved in this process. Others argue that the neuroglia are also involved, as they were found in rows extending from the nerve ends; while fibroblasts contribute to the formation of connective tissue where these cells are included in these rows. As a result of this activity, in each divided nerve ending, consisting of an edematous and disorganized matrix of neuroglia and fibroblasts alongside capillaries, macrophages, own connective tissue cells, and collagen fibers, a swelling was observed. The neoformed capillaries penetrate from the nerve ends of perineural vessels to the point of the injury.

The degree of collagenization is important in this type of injury, because the synthesis of this is important in the neural layers surrounding regeneration of axons. Likewise, from the histological point of view there is an increase in the number of nuclei, mainly due to the proliferation of neurilemma cells, and a large increase in collagen (Sunderland, 1985).

In the biochemistry of regeneration, the various enzymes involved allow structural and metabolic phenomena to occur. After nerve regeneration, approximately 40% decrease in fosfocreatina was observed by Bodian & Mellors (1947). With the reinnervation of the distal nerve section, enzymes and lipids of myelin, such as alkaline fosfomonoesterase and aliphatic esterase, reappeared. At the same time, a reduction associated with the nucleic acid content and the activity of enzymes (Sunderland) was observed. Pinner *et al.* (1964) also reported on the restoration of normal alkaline phosphatase as regeneration progressed and associated this with the

remyelination of the membrane of the neurilemma cells. A phenomenon that indicates the high metabolic activity of the cell during this process is that axons did not deposit glycogen because of the necessary increase in protein synthesis.

The speed of regeneration of a divided axon depends on several factors, including the severity of the injury and the distance between the extremities. In addition, depending on the nature of the injury, the speed is slower after the nerve is sutured, which escaped injury after the wall of the endoneural tube was injured, i.e., regeneration would be faster than the nondegenerated layers of tissue that surround the axons (Huang *et al.*, 1992). It depends on the size and type of the fiber. Gutman (1986) states that the sensory fibers regenerate at greater speed than motor fibers. They explained this by stating that "to be or not to be myelinated in the finest motor, needed less time to get a full functional repair." Other factors were age, chemical, temperature variations individual species, and effects of a second injury on the neuronal regeneration.

A photostimulant effect is achieved by applying laser, which is the amplification of light emission excited by radiation; this produces "non-ionizing rays of light, very intense and monochrome," which are aligned and are consistent (Karu, 1987; Shin *et al.*, 2003).

At present, complete awareness on the mechanism of the action of laser does not exist, but it is believed that it modulates cell behavior without significantly increasing tissue temperature. The activity on the tissues is not due to thermal effects, but due to the interaction of electromagnetic waves with the cells. The energy absorbs fluid where the concentration is higher, and therefore there is an increased uptake in the inflamed edematous tissue, stimulating many biological reactions related to the process of repairing the wounds. There is an interaction between photons and irradiated cells (photochemical reaction); the cell absorbs the energy of the photon and the energy transferred would depend on the power of penetration of the beam, causing an increase in kinetic energy that activates or deactivates enzymes or other physical or chemical properties of major macromolecules. The exact mechanisms that underlie this process are still unknown and are being studied by the scientific community (Oltra-Armon *et al.*, 2004).

The unlikely damage to tissues due to energy emission is characterized as a beneficial tool, both in

medicine and dentistry. It is possible to find various applications of energy emission, the most important being an effective and trophic biostimulant in tissues; it is also capable of stimulating the formation of collagen and elastic fibers, neoplasm of blood vessels, cell proliferation, and osteoblastic cells. There have also been investigations where direct nerve regeneration has been observed, as well as an increase in the speed of regeneration. Energy emission can be also applied in therapies, either locally because it has an anti-inflammatory action and is anti-edematous or to promote blood circulation and analgesic action (Walsh, 1997).

The biological effects of laser radiation of which we can mention its anti-inflammatory action, anti-edematosa, and its stimulating effect on cellular metabolism, as well as fibroblastic proliferation and stimulating action of the immune system, leading to increased production of antibodies are known. As a result of these effects, there is less discomfort to the patient and the healing process is accelerated. There are different types of lasers in dentistry, which can be divided according to its power and its purpose (España-Tost *et al.*, 2004). We must distinguish between two large groups of lasers: the high-powered or the surgical laser and the low-yield or the so-called therapeutic laser (Oltra-Arimon *et al.*).

High Power Laser can be used on hard tissues; it has high energy, emits an invisible light, and has thermal effect, because it is capable of focusing high energy in a very small space and this is demonstrated by its cutting capacity, vaporization, and coagulation (Oltra-Arimon *et al.*). Among them, erbio-yag, neodymium yag, eximer, and CO₂ are well known and are used in hard tissues in dentistry, for example, for the removal of cavities as well as for making incisions in mucous membranes and in soft tissue sterilization (España-Tost *et al.*).

Low Power Laser, used in soft tissues, has low energy and is in the spectrum of visible light; it lacks thermal effect because the power used is low and there is more surface action; hence, the heat dissipates, producing further biostimulant effect on cells. Its implementation is essential in accelerating tissue regeneration and healing, and in diminishing inflammation and pain (Oltra-Arimon *et al.*; Suazo *et al.*, 2007). This type of laser causes proliferation, differentiation and death, but the cellular mechanism is not completely known (Wu *et al.*, 2007). Another application can be addressed, for example, to minimize postoperative inflammation after surgery. This fact can

be defined as characteristic of a low-power laser (Oltra-Arimon *et al.*).

There are several traded low-energy laser units of which the laser Arseniuro and Aluminum Gallium (Ga, Al, As) are important. Aluminum Gallium is a continuous laser with a wavelength of 830 nm, which can operate with a maximum power of 10 W and is transmissible by fiber optics. Laser Arseniuro of Gallium (Ga, As) is a pulsed laser with a wavelength between 650 and 950 nm (the most common is 904 nm laser-Helium Neon emitted in the visible spectrum, including the red at 632.8 nm) (Oltra-Arimon *et al.*). There are two interesting lasers: the infrared laser and the Helium-Neon (He-Ne). The latter has a healing effect, is antialgic and a biostimulant (España-Tost *et al.*).

The depth of the energy of this laser in bone tissue is 1cm, while in soft tissue it may vary from 2 to 5 cm. There are differences in the application of a type of laser with respect to the other, although the high-power laser is used for surgical purposes, the problem is that they dissipate the heat generated as well as inhibit intracellular metabolic processes. The low-power laser was used rather late as anti-inflammatory and antialgic, essentially acting in histic repairing, increasing cell proliferation, in the production of collagen and elastic fibers, alkaline phosphatase, in the regeneration of nerve fibers and bone tissue, increasing the speed of growth of blood vessels, and in the induction of reepithelialization of the epithelial cells adjacent to the lesion. As a result, speedy and complete repair of the damaged tissues can be achieved (Suazo *et al.*).

The effect of low-power laser on various oral tissues has been studied by several authors, thereby recognizing the beneficial effect on wound healing of the oral mucosa and other tissues. Its action is based on cell multiplication, the formation of collagen and elastic fibers, and reepithelialization of the damaged tissue; on vascular endothelial cells, increased mitotic activity occurs rapidly and buds or outbreaks of vessels are available for the neof ormation of microvessels. The use of low-power laser is associated with the increase in microirrigation, mediated phenomena of angiogenesis, and with increases in the irrigation of the distal portion of a flap irradiated with low-power laser (Suazo *et al.*).

Among adverse effects, which are rare, caused by the use of low-power laser is increase in pain that usually disappears. It must be pointed out that very few studies refer to the adverse effects caused by the application of LLL therapy (Oltra-Arimon *et al.*).

MATERIAL AND METHOD

A meta-analysis of literature available through secondary sources of information was carried out. We analyzed papers or research papers that were obtained through EBSCO and PUBmed. The criterion for inclusion was that the work should have used low-power or high-power laser. The work should have investigated the effects of laser on the peripheral nerves in animals. Other requirements are that all the works should have used a control group as the main reference in arriving at conclusions and results, the sample should have been significant, and that this type of study on animals should be applicable to humans too. Key words used to locate this kind of research were nerve regeneration and laser.

RESULTS

In previous research, the implementation of laser to stimulate nerve regeneration has been effective; several works describe the trophic and biostimulant action of this treatment.

According to the study, Garrido & Valiente found that this instrument generates a stimulus for healing by stimulating the synthesis of collagen and elastic fibers, which were found in cultures of fibroblasts; DNA activation and subsequent formation of precollagen fibers of type I and III were also noted. It was also found that the number of mitochondria increased in cells and the endoplasmic reticulum showed dilation, which showed a higher cellular activity.

The neoformation of blood vessels has been observed; an increase in mitotic activity occurring during outbreaks from existing ones (angiogenesis) and generating formation of microvessels have also been observed. The work of Kipshidze *et al.* (2001) attempted to determine the effect of irradiation, levels of vascular endothelial growth factor (VEGF), and the proliferation of *in vitro* endothelial human cells; this was carried out through different doses of application. The study then showed that the use of this type of laser increased VEGF synthesis in muscle cells, fibroblasts, and cardiac myocytes; it also stimulated the growth of endothelial cells in culture.

It causes stimulation in the repair of bone tissue. In cell cultures of the clonal bone, as observed in

fibroblasts (Almeida-Lopes *et al.*, 2001), there was an increase in the activity of DNA and as a result an increase in osteoblast cells proliferation. Likewise, the results showed an increased presence of the alkaline phosphatase enzyme (essential in the process of mineralization). The effects of the laser were tested by radiographs, because of the irradiation of a high density area. It is postulated that these areas are photoactivated first and then the ultrasonic wave is generated by the laser pulse (Garrido & Valiente).

The laser has a positive effect on pain and inflammation. Its antialgic action "is based on the normalization of the tissue concentration of substances, interfering with the message electric nerves sensitive to normalize the membrane potential, as well as acting on the filter core." In the first two applications for acute inflammation, there is an expected decrease in the swelling, "given the rapid action vascular produced by the laser in the area where it is absorbed (Mier, 1989)." If the inflammation is chronic, the response of the vascular tissue will be slower and will require a greater number of applications or even a reduction in the structures affected.

With regard to nerve regeneration, Garrido & Valiente, in their review of the literature showed that "investigations of facial nerve divided experimentally in mice and in human medial nerve, brought success in implementing low-power laser." Mester *et al.* (1985) described that one of the clear effects in terms of trophic action of the laser is the acceleration of nerve regeneration in the divided axon, especially in post-traumatic neuropathy. Belkin & Schwartz (1994), in their study, discussed the bioeffect on the nervous system, which "are manifested as alterations in the biochemical constituent and cellular and extracellular reactions, as well as changes in the rate of cell division." They state that the laser produces antialgic effect and also postpones the processes of post-trauma cell degeneration, as clinical effects.

In a study by Shamir *et al.* (1995) (there was a similar pilot study), after the section and anastomosis of the ischiatic nerve, transcutaneous LLL was used on the relevant parts of the spinal cord and the peripheral nerve. Histologically, there was an increase in the number of axons and the diameter along with a better quality of regeneration. "The study suggested that the use of post-surgical LLL boosts regeneration process in peripheral nerves after his comprehensive section and suturing."

The laser then exerts an effect on the healing and regeneration of nerve tissues, primarily through its stimulation of fibroblasts and an increase in protein synthesis and collagen (connective tissue stimulates) in the first stage of regeneration (inflammation) followed by the "activation" of the cell. In addition, an increase in mitotic activity of the blood vessels in the peripheral nerve allows access to the substrate.

Alkaline phosphatase, an enzyme, is present in nerve regeneration, in remyelination, and in the neurilemma cells of the membrane; the laser increased levels of this enzyme in the bone tissue, thus stimulating this process, but no scientific evidence has been found that the same process would occur in the nerve tissue. The laser should accelerate the healing process to have a positive effect on inflammation, thereby leading to regeneration and reducing the total time of recovery in the event of sensory nerve damage; however, great importance is attached to the stage at which the laser is applied. If applied in the early stages of inflammation or early days of the occurrence of the damage, then the effect is different from that when applied at a later date.

Clearly, other papers noted that the process of nerve regeneration was more efficient, better, and faster in the experimental group than in the control group and was tested by the presence of both an increase in the rate of cell division, changes in biochemical constituents, cellular reactions, and there was also an increase in the number of axons, which also had a larger diameter.

It has been found that the levels of some growth proteins are elevated following the implementation of LBP. Shin *et al.* observed the therapeutic effect by analyzing levels of the growth-associated protein GAP 43, which is involved in the normal processes of nerve regeneration. In previous work, rats with the same type of injury were irradiated with laser for four consecutive days. Later, immunohistochemical analysis was performed using antibody GAP and 43, which showed that the LBP might have an effect in the early stages of the process of regeneration.

Rodriguez *et al.* (1996) carried out an experimental study with 72 rats, which were divided into four groups, where group I was the control group, He-Ne laser was applied on group II, xenon light on group III, and solar light on group IV; the ischiatic nerve was previously divided and sutured in all the rats. The results showed that 20 rats in group I had trophic lesions (loss

of phalanges, fingers complete, and plantar ulcers) and motor disorders, which remained until day 15 and 20 and disappeared after that time. In groups II and III, only 2 rats showed loss of nail or phalanx. Of all, group IV presented trophic lesions and motor disorders. Histopathology in groups I and II showed axonal and myelin damage equal to 15 days, but from that day group II presented "a greater number of axons and reorganized mielinizados well." Unlike the other 3 groups, group II presented an increase in the number of neoformed vessels from the first day.

Shi *et al.* (1997) found an increase in the speed of axonal regeneration in spinal motor nerve cells in rabbits. Some axons were regenerated at 4 weeks in the group irradiated with He-Ne laser, while it was evident at 8 weeks in the non-irradiated group. Also, the regeneration of myelin sheaths and greater muscle control was evident. Thus, a conclusion was reached that this type of laser "certainly promoted the operation of the peripheral nerves and accelerated axonal regeneration."

Further, Rochkind *et al.* (1989), in their study, sought to determine the response of a damaged nerve in rats before implementing the same type of laser (He-Ne). It was found that this had an effect on its nervous activity; there was an increase of action potentials of 33% after the first transcutaneous irradiation. It was also observed that scar tissue decreased in areas irradiated when compared with the control group.

The literature indicates that the He-Ne laser would be beneficial both to encourage and to accelerate this process. All investigations showed significant differences in greater regeneration in experimental groups, but results differed on the time taken to begin regeneration, as in the study by Rodriguez *et al.* They observed changes from day 15, whereas in the study by Shi *et al.*, changes could be determined by the dose applied only at 4 weeks. Also, the authors postulated an increase in the action potentials, suggesting not only a regeneration of the nerve structure but also an effect on the functioning of the nerve and its dominance after an injury. One factor that would clearly stimulate this element is the ability to modulate neurilemma cells essential for the growth of the axon.

The effects of the application of low-power laser He-Ne and some differences from other types of low-power laser can be observed through different works. Khullar *et al.* (1995) carried out an injury in the standardized ischiatic nerve in rats, achieving axonal

degeneration. A group of 10 animals was treated with laser GaAlAs for 28 days. The other 10 animals formed the non-irradiated control group. It was finally noted that the experimental group had a higher functional recovery of the nerve than the second group, but no difference was observed with regard to the action potentials and there were no morphological differences between groups, which was justified by saying that "effects of low level laser therapy should have happened more peripherally to the measuring point."

Bae *et al.* (2004), in their study, used infrared laser (Ga-As) transcutaneously in the damaged ischiatic nerve. After the trauma, action potentials and speed of regeneration decreased significantly; however, these parameters recovered after the application of the treatment. The results suggest that the low-power infrared laser irradiation can improve the mechanical damage in the ischiatic nerve and stimulate the regeneration of nerves. However, a similar study described by Comelekoglu *et al.* (2002) found no significant differences in the amplitudes of action potentials or speed of regeneration between the experimental group and the control group. Bagis *et al.* (2002), in their study, also used this type of laser and arrived at the same conclusion that "the irradiation of low-power laser Ga-As at 42 different intensities between 0005 and 2.5 J/cm² does not generate impact on action potential and nerve excitability." Research on low-power laser (excluding the He-Ne) indicates no significant difference between the control and the experimental groups. Although there are works that affirm the hypothesis, others contradict; therefore, there is no convincing evidence that low-power laser is totally effective, although morphological changes may not generate differences in the action potentials.

Several work using high-powered lasers have been submitted; however, the results differ from low-power lasers. Menovsky & Beek (2003), in their investigation, used CO₂ laser. They carried out section of ischiatic nerves of 8 rats, which were sutured and fused by the CO₂ laser and a welder protein (bovine serum albumin) was also added as reinforcement. In the control group, the nerves were sutured using a fibrin sealant. In the other 8 rats, conventional sutures were applied. It was noted that "the motor function of the three groups showed an improvement over time." At 16 weeks, motor function was approximately 60% of the normal function and there were no significant differences between groups. In histological studies, all the nerves revealed varying degrees of regeneration, with myelin sheaths in the distal segments of the nerve. There were

slight differences in favor of the group treated with laser, in terms of healing of the wound. "It was therefore concluded that repair nerve assisted with CO₂ laser welding is at least equal to fibrin sealant and conventional sutures in the rodent ischiatic nerve."

Ochi *et al.* (1995), in an attempt to improve the performance of this type of laser, implemented another method, which applied CO₂ along with a fibrin membrane to ensure efficiency, and compared it with the conventional method of suturing. The result was that "there were deleterious effects of irradiation, in terms of nerve regeneration, at any time after surgery. The number of myelinated axons greater than 5 µm in diameter and the diameter at 8 weeks after surgery was significantly higher in the irradiated group than in the suture group. These results suggest that this new method may be useful and effective to repair nerve in clinics."

In regard to the high-powered laser, there is no significant evidence of its effect on regeneration; in the literature, in addition to the laser, supplements such as bovine albumin or fibrin membrane have been found to be used. It is not known who actually produced the result. There were no major differences with the other groups, although there were differences in the study by Ochi *et al.* It is not possible to determine whether the effect is by the laser or generated by the fibrin membrane.

DISCUSSION

Through a review of the various studies, it can be stated that the low-power laser clearly has biostimulant and trophic effects on nerve cells and is therefore able to stimulate and speed up the process of nerve regeneration after section and posterior suturing of the peripheral nerve. It is also possible to conclude that the low-power laser He-Ne brings greater benefit as already observed. Significant differences and relevant results indicate stimulation of the tissues, thereby promoting the laser's functionality. Other low-power lasers do not prove to be as effective, because the work was contradicted on outcomes rather than apparent improvement in the functioning between the experimental and the control groups. It is possible to assert that among the types of lasers, depending on their power, the high-powered ones do not bring great benefits at this point. There is no conclusive evidence on their claims. Moreover, the work presented biases that ultimately invalidated the findings.

The laser increases the effectiveness of treatment and reduces the recovery time of the patient, and the time taken would be a good adjunct therapy.

One of the problems faced during research, is that the studies have been conducted on cells in vitro and in animals, but none in humans, which shows that much remains to be studied in this regard. There is a long way to go in order to implement this therapy in medicine and dentistry, since the results are not yet conclusive in all respects. Therefore, it would be interesting to conduct an investigation in this regard and apply it in humans, in order to observe actual results. It can be concluded the low-power laser would be a useful tool in dentistry because of its wide range of applications and the many advantages as presented in the review.

While this issue has been investigated, it has not been widely discussed. In dentistry in recent times, the laser has been implemented in some specialties, but one does not really know all the options and benefits that it can bring. We can say that this subject is not well known to many because of unknown utilities. However, it would be very useful as a therapeutic, especially for nerve recovery after maxillofacial surgery, which can affect the sensitivity of the patient. It could also be used in inflammation, bone regeneration, and other stomatognathic system pathologies. However, the incorporation of laser in dentistry should be conservative because it is not the solution for all cases, and conventional techniques besides being cheaper cannot be replaced by the laser, but this can be rather used to complement other techniques, which would bring great benefits and allow us to pursue a much less invasive dentistry.

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RESUMEN: La aplicación de láser como medio terapéutico en la regeneración nerviosa en odontología, no ha sido un tema muy discutido, aún cuando el conocimiento de la respuesta del sistema nervioso periférico es muy importante tanto en la práctica como en la recuperación del paciente. Se ha propuesto que el láser de baja potencia (LBP) tiene efectos benéficos en los tejidos, entre ellos antiálgico, antiinflamatorio, antiedematoso, anticelulítico y bioestimulante del trofismo celular. En el presente estudio se realizó un metaanálisis de la literatura disponible en relación con la respuesta del nervio lesionado ante la aplicación de láser de baja potencia utilizando los buscadores EBSCO y PUBMED. La literatura se refiere al efecto estimulante del LBP en la neoformación de vasos y existiendo evidencia bibliográfica para proponer a este mecanismo como importante en la regeneración nerviosa. Los efectos del láser de baja potencia en Odontología presentaron una escasa evidencia bibliográfica.

PALABRAS CLAVE: láser de baja potencia, láser, odontología, regeneración nerviosa.

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