Abstract:

Laser therapy (LT) acts when the photons of particular wavelengths interact with certain molecules or chromophores of the tissues. This process is called photobiomodulation and determines the clinical effects of LT, such as increased tissue healing, enhanced blood and oxygen supply to the area, analgesia and immune modulation. Wound healing with LT is faster, stronger and has less risk of complications. The treatment is also indicated for infected wounds and, together with the increased oxygenation, enhanced phagocytic activity and less inflammation of the area, there is a direct antimicrobial effect. This allows the veterinarian to decrease the use of antibiotics in practice and can represent a crucial resource to treat multiresistant infections. Because of the different and multiple parameters involved in each laser treatment, published studies can be difficult to compare, and although it is clear LT is effective on infected wounds, more research is needed to determine the best parameters for each microbial species and clinical situation.

Keywords: laser, photobiomodulation, wound, infection, antimicrobial

LASER therapy (LT) has become part of many practices’ treatment for wound care and could become the gold standard in the near future.

The biological action of the laser light is due to its absorption by certain molecules of the tissues called chromophores (from the Greek meaning transporters of the colour). The wavelength (nanometres; nm) or colour of the emitted light determines the chromophore that will be targeted, as well as the ability to penetrate the tissue - we are more transparent to infrared light than to visible light. LT works in the red and infrared electromagnetic spectrum (about 660nm to 1,000nm) and therefore is non-ionising radiation.

The main chromophores are water, haemoglobin, melanin and the cytochrome C oxidase enzyme that is at the end of the mitochondrial respiratory chain and is ultimately responsible for the generation of adenosine triphosphate (ATP). This molecular interaction with light produces an improvement in the release of oxygen into the tissues, microgradients of temperature that enhance blood flow and, eventually, an increase in ATP production through aerobic metabolism. As a consequence, there is the induction of transcription factors and increased cell proliferation, mobility and extracellular matrix deposition, among others. Clinically, this manifests as:

- improved vascularity to the treated site;
- increased tissue healing; and
- anti-inflammatory and analgesic effect.
Among all the effects, wound healing is probably the most documented one. It has been demonstrated in vivo and in vitro - both with healthy fibroblasts - and on diabetic cultures/patients\textsuperscript{1,2}. Together with improved wound healing, the antimicrobial potential of LT is being studied and has been demonstrated even with methicillin-resistant Staphylococcus aureus (MRSA).

As a general mechanism, enhancing blood flow and oxygenation to a diseased area will help tissue healing. The effect of the laser on blood flow is extended after the exposition to light has finished. It is supported by an increased angiogenesis promoted by basic fibroblast growth factor and vascular endothelial growth factor\textsuperscript{3,4}.

Laser increases fibroblast multiplication, differentiation and motility, as well as collagen production, which will produce an earlier wound closure\textsuperscript{5}. The collagen generated under LT has a higher percentage of type III\textsuperscript{6}, which builds up stronger, but less exuberant, scars. This, mid-term and long-term, provides a higher tensile strength with better tissue malleability and less local discomfort\textsuperscript{14,15}.

These benefits in wound closure apply to clean surgical wounds, second intention healing\textsuperscript{9}, graft and flap survival\textsuperscript{10,11}, and contaminated and infected wounds\textsuperscript{12,13}. The increased oxygenation also helps with most infections, since pathogenic microorganisms often grow poorly in an oxygen-rich environment.

LT also has more indirect effects to treat infection: it enhances macrophage function and modulates immune response and reactive oxygen species production\textsuperscript{14,15}. There is also a potential direct effect on microorganisms that has put more focus on LT as a non-pharmacological antimicrobial tool, also due to the increasing antibiotic resistance problem world-wide. The research concerning this use for infected tissues can be separated into in vitro assays with microbial cultures, and clinical trials with experimental infections (plus clinical reports about spontaneous infections).

In vitro studies have not yet fully elucidated the underlying mechanisms of the antimicrobial effect and have provided different results - most experiments seem to show a decreased microbial growth after exposition to laser light, including common pathogenic and opportunistic species such as \textit{S} aureus\textsuperscript{16}, MRSA\textsuperscript{17}, \textit{Escherichia coli}\textsuperscript{16}, \textit{Pseudomonas aeruginosa}\textsuperscript{18} and \textit{Candida albicans}\textsuperscript{16}, but a few of them show no effect\textsuperscript{16} or even an increased bacterial growth\textsuperscript{18}.

Some aspects have to be considered when reviewing these papers, such as the different parameters used in each of them (for example, different wavelength, energy density, power density and so on) and the different metabolism and kinetics of a bacterial culture when compared to a full in vivo infected tissue.

In vivo experiments (as well as case reports) have provided consistent and encouraging results to support laser use in infected tissues, including infections with MRSA\textsuperscript{20,21}, non MRSA, \textit{E coli}\textsuperscript{13} and \textit{P aeruginosa}\textsuperscript{12,22}. These results seem to be consistent despite the different technical parameters we of course find when comparing in vivo studies too.

All mentioned therapeutic effects take place at physiological temperatures\textsuperscript{16}, so if the laser is properly used the patient never experiences any thermal discomfort; on the contrary, LT increases endorphin release and has a potent analgesic effect\textsuperscript{23}. 
There are no secondary effects after LT; it cannot be used over tumours - since we are stimulating cell proliferation and neovascularisation - or active bleeding sites, but if handled properly (eye protection, correct training and so on) it is an extremely safe therapy.

From a practical point of view, doses used for wounds usually range from 1J/cm$^2$ to 5J/cm$^2$ for acute ones, but for chronic cases, sometimes up to 20J/cm$^2$ to 30J/cm$^2$ is needed.

In the author’s experience, the best dose for each case is determined starting on the conservative side, and by adding up to 50 per cent to 100 per cent more every two treatments if required. To effectively deliver such dosages to a wide area (the wound plus at least 2cm to 5cm margin of ealthy tissue) in a clinically reasonable time, and to be able to reach deeper structures when needed, a class IV laser is recommended. Class IV indicates the average power of the laser is above 0.5W (500mW). Since power represents energy delivered over a certain time, the more power we have available, the shorter treatments can be, and more photons will penetrate in depth (provided the right wavelengths are used).

**Examples of laser use on patients with multiresistant wounds**

**Case one**

A four-year-old female, spayed Portuguese hound under treatment with cephalaxin plus metronidazole plus ciprofloxacin and carprofen for three weeks after surgery for hip fracture and traumatic abdominal hernia - the last repaired with a polypropylene mesh. The animal presented with pain, decreased activity level, 30 per cent of bodyweight loss (in three weeks), abdominal wound dehiscence (12cm) and inflammation (**Figure 1**). The blood culture was negative. It was treated at the Hospital Clinico Veterinario Complutense in Madrid, with a total of eight sessions over two weeks (**Figures 2 and 3**). Initial doses were 4J/cm$^2$, a gradual increase over the treatments up to 10J/cm$^2$. An ibiotics and NSAIDs were discontinued after the first week of laser treatment.

![Figure 1. Case one: a four-year-old female spayed Portuguese hound before laser therapy (day 0).](image1)

![Figure 2. The same dog as in Figure 1 after 48 hours and two treatments later.](image2)
Case two

A six-year-old female, spayed mixed breed dog with multiresistant (cefovecin, amoxicillin, ampicillin, cephalaxin, gentamicin, doxycycline, ciprofloxacin, enrofloxacin, marbofloxacin and an ongoing list) Klebsiella pneumoniae with secondary Candida infection susceptible to amikacin, which was administered. Three weeks and four surgeries after an initial procedure for a digestive foreign body, the patient was referred to Integra Centro Veterinario en Majadahonda, Spain for laser treatment of a dehiscent laparotomy wound (Figure 4). Initial doses were 4J/cm², with gradual increases over the treatments (Figures 5 and 6) up to 15 J/cm² - a total of 10 treatments.

Both cases were treated with a K-Laser Cube 3 device using three wavelengths simultaneously: 660nm, 800nm and 970nm. In both cases, the continuous wave was combined with pulsed light, since this delivery mode with pulses of different frequencies has been proposed to be beneficial.
Summary

In some cases, laser will be an adjunct in your global treatment protocol that will help you shorten or avoid antibiotic therapy, enhance wound healing and provide a stronger scar. In others, laser will be one of the few resources available for multiresistant infections and for animals with a low tolerance for antibiotics. In any of these, it will make a significant and consistent difference in your patients. (Please note some drugs in this article are used under the cascade).
References


