The low-level laser therapy on muscle injury recovery: literature review

A terapia laser de baixa intensidade na recuperação da lesão muscular: revisão da literatura

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Abstract

The muscle injury recovery process is slow and often changes the original mechanical properties of the damaged muscle. The goal of rehabilitation is to recover the muscle as fast as possible offering the lowest risk of injury recurrence. Among the available therapeutic resources, the low-level laser therapy (LLLT) has proven to be effective both in reducing the deleterious effects of the acute inflammatory response, as in the stimulation of the events involved in the repair phase of the muscle recovery process.

Descriptors: Muscles/injuries; Physical therapy; Laser therapy, low-level; Rehabilitation

Resumo

O processo de recuperação de uma lesão muscular é lento e muitas vezes alteram as propriedades mecânicas originais do músculo. O objetivo da reabilitação é recuperar o músculo o quanto antes oferecendo o menor risco possível de recorrência da lesão. Dentre os recursos terapêuticos disponíveis, a terapia laser de baixa intensidade (TLBI) tem se mostrado extremamente benéfica, tanto na redução dos efeitos deletérios da resposta inflamatória aguda, quanto na potencialização dos eventos envolvidos na fase de reparação do processo de recuperação da lesão muscular.

Descritores: Músculos/lesões; Fisioterapia; Terapia a laser de baixa intensidade; Reabilitação

Introduction

The main goal of rehabilitation in muscle injuries is to bring the person back to physical activity as soon as possible offering the lowest risk of injury recurrence[1]. To achieve this goal, the physiotherapist relies on a wide range of therapeutic resources which can be used as tools to accelerate the muscle recovery process and promote the balance between scar tissue formation and muscle regeneration in a way to provide both strength and torque to the recovered muscle[2-4]. Among the available resources, the low-level laser therapy (LLLT) has been proven to be effective both in the modulation of acute inflammatory response and the secondary damages produced by it, as in the stimulation of cells involved in the repair phase of the muscle recovery process[5-6].

Literature review

Muscle injuries

Muscle injuries can be caused by different mechanisms and constitute a major challenge the rehabilitation[7]. Depending on the mechanism of injury and its symptoms, muscle injuries can be classified in contusions, sprains, lacerations[8-9] and those induced by exercise[10]. However, regardless of the mechanism that caused the damage, the muscle recovery process always follows the same path involving specific events that overlap each other: degeneration, inflammation, repair and finally, remodeling[8,11].

Degeneration phase

The degeneration phase begins with the rupture of the basal and plasma membranes of muscle fibers by the mechanism of injury, allowing an influx of extracellular calcium and consequent activation of intrinsic proteases that cause the autodigestion and necrosis of the broken fibers[12]. On the other hand, in the moments following the injury, a condensation on the cytoskeletal of the broken fibers form a band of contraction which acts as a buffer, preventing the degeneration to spread along the fiber and limiting the injury to a local process[8,11].

Inflammatory phase

The first inflammatory signs of a muscle injury may be noted from the time that some proteases and enzymes such as phospholipase A_2, are activated by extracellular calcium influx. The phospholipase A_2 cleaves the arachidonic acid from phospholipids present in the sarcolema of the disrupted muscle fibers. In its free form, arachidonic acid may follow two different pathways. One of the leukotrienes, that act on leukocyte chemotaxis and increase of vascular permeability, and another of cyclooxygenase, which produces prostaglandin E_2, a substance that increases vascular permeability and pain sensitivity in the injured area[12-13]. The first immune cells to reach the site of injury are the neutrophils, though their presence tends to decrease as the population of macrophages increases in the next couple of days following the injury[7-8,12]. Besides being responsible for the phagocytosis of necrotic material resulting from the inflammatory process, neutrophils and macrophages release important chemical factors that operate in the recruitment of satellite cells which participate actively in the muscle tissue regeneration[8,11]. On the other hand, the release of reactive oxygen species due to the neutrophils respiratory burst may increase the acute inflammatory response, damaging adjacent healthy cells and expanding the area of injury[8,13]. The death of healthy cells during the acute inflammatory phase of muscle injury also occurs by secondary hypoxia due to the ischemia caused by the rupture of blood vessels, increased blood viscosity and occlusion of capillaries caused by increased extracellular pressure[14].

Repair phase

The repair phase of muscle injuries is marked by two simultaneous processes, the regeneration of broken fibers and the formation of scar tissue, so the balance between these two processes is essential to preserve the original mechanical properties of the inju-

red muscle[2,4,11]. The muscle regeneration occurs through the attraction of satellite cells by chemical factors to the injury site, where they differentiate into myoblasts to then merge into myotubes and finally mature giving rise to new muscle fibers that fill the space between the broken fibers[9,15]. It's not always that the regenerated muscle fibers reconnect to the remaining segments of the broken fibers, instead they tend to adhere to the extracellular matrix of scar tissue interposed between them[9]. The formation of scar tissue starts with the formation of a scaffold of fibrin and fibronectin that acts as anchorage site for the fibroblasts[4,11,15]. This structure grows as the fibroblasts firstly synthesize and deposit the fragile fibers of collagen type III and later the fibers of collagen type I, which is more resistant but less flexible[4,11]. The formation of extensive fibrosis is a limiting factor in muscle recovery process, since the excess of scar tissue hinders the regeneration of muscle fibers and reduces both the extensibility and contractility of the injured muscle[12,15].

Remodeling phase

The last step in the muscle recovery process is the remodeling phase. At this stage the regenerated muscle fibers contract as the collagen fibers reorganize themselves[15] according to the tensions imposed to the muscle. These tensions are extremely important since they enhance the adhesion of regenerated muscle fibers to the extracellular matrix[4] and contribute to reduce the final amount of scar tissue[2,4].

The LLLT

The LLLT refers to the use of monochromatic and coherent light beams at specific wavelengths able to induce photobiological reactions when absorbed by photoreceptor molecules known as chromophores present in the irradiated body tissues. The photons contained in the laser beam has the ability to change the structure of chromophores, leading them to electronically excited states that trigger biological processes at cellular level[5,16].

LLLT on ATP synthesis

In muscle fibers that had its cellular structure compromised by an injury it has been observed a reduction in the population of mitochondria[17], besides the hypothesis that calcium influx caused by rupture of the sarcolemma also inhibits mitochondrial respiration, reducing in both situations the availability of intracellular adenosine triphosphate (ATP)[16,18]. An analysis of the integrity of intracellular ATP allows the evaluation of the physiological status of the cell, its energetic properties, metabolic regulation and also the functionality of its signaling system which is responsible for coordinating several cellular functions[19]. The photons from LLLT change the molecular conformation of some metal components present in the enzymatic complexes of the mitochondrial respiratory chain increasing significantly the transfer of electrons along the respiratory chain and the pumping of protons across the inner membrane of mitochondria, what enhances significantly the ATP production[5,20]. The increased availability of ATP provided by LLLT reactivates cellular processes that were inhibited due to the physiological changes triggered by muscle injury, such as the synthesis of DNA, RNA and proteins which play an important role in the cell proliferation and muscle recovery processes[19-20].

LLLT on the oxidative stress

In a study that compared its anti-inflammatory effects with those provided by common cyclooxygenase inhibitors drugs, LLLT was able to reduce reactive oxygen species both directly as through the antioxidative activity of the superoxide dismutase enzyme, which decreases the expression of cyclooxygenase reducing the release of prostaglandins and modulating the inflammatory response[21]. Although it is known that neutrophils play a key role in the muscle recovery process, the huge increase in reactive oxygen species due to the neutrophils respiratory burst during acute inflammation may damage some vital cell constituents, such as proteins, lipids and DNA itself, what hamper the muscle recovery process and harm adjacent healthy cells, increasing the area of injury[7,17,22]. However, reactive oxygen species cannot be seen just as aggressive agents, since they also act as important secondary messengers in several physiological functions of the cell, such as DNA synthesis and cell proliferation[5]. The proper application of LLLT is able to reduce excess reactive oxygen species without compromising cell viability, positively influencing the resolution of the inflammatory process[22].

LLLT fibroblast proliferation

Fibroblasts have a wide range of chromophores that can be stimulated by different wavelengths of LLLT[23], increasing the release of basic fibroblast growth factor (FGFb) and insulin-like growth factor (IGF-1) produced by these cells. These substances are essential for the tissue repair process, since they stimulate both the proliferation and the recruitment of new fibroblasts, enhancing the synthesis of collagen and contributing to the formation of new blood vessels and important elements of the extracellular matrix[24].

LLLT on muscle regeneration

The satellite cells remain quiescent beneath the basement membrane of muscle fibers and play an important role in muscle regeneration, where they give rise to new fibers that replace those ones that were damaged by the mechanism of injury[25-26]. Both in vitro[26] as *in vivo*[6,25] studies have confirmed that LLLT favors the regeneration of muscle tissue through the activation of satellite cells by introducing them in the cell cycle that promotes its proliferation and progression to the status of new muscle fibers[6,25-26].

Discussion

It is important to take into account that the biological effects observed in the tissues submitted to LLLT depend directly on the adopted parameters for its application[6,20,27-28]. The radiant power of the laser device in Watts, the cross-sectional area of the laser beam in square centimeters and the irradiation time in seconds, are the basic parameters used to calculate two other parameters that reflect the dose applied: (1) the energy density in Joules per square centimeter, which is the result of the irradiation power multiplied by the irradiation time and divided by the cross-sectional area of the beam; (2) the radiant energy in Joules, which is obtained by multiplying the device radiant power by irradiation time[27]. The radiant energy is probably the most influent parameter in the treatment outcome since it represents the total amount of measurable energy inherent to the photons deposited on each irradiated point[27].

Regarding the wavelength, both anti-inflammatory and biostimulatory effects of LLLT may be obtained from different wavelengths between 630 nm and 1064 nm[29]. The infrared lasers have greater penetrating power so that a significant portion of its photons can reach deeper body tissues. In contrast, red-light lasers are more advantageous in the surface layers, since most of its photons are absorbed by tissues located at this depth[25,27].

In the application of a single dose of LLLT (660 nm; 100 mW; 0.03 cm^2; 40s; 4J) after a model of exercise induced muscle injury in rats, biological samples collected between 24 and 48 hours after irradiation showed a significant reduction both in creatine kinase levels, a biomarker for muscle damage, as in the number of cells that died by apoptosis[16]. The LLLT (632.8 nm; 0.5 cm^2; 600s) with different radiant power of 4 mW; 9 mW and 14 mW, obtaining doses of 2.4J; 5.4J and 8.4J respectively, applied after an injury induced by eccentric muscle contractions in rats, promoted an increase in the antioxidative activity and a significant reduction in the inflammatory response. Nevertheless, the doses of 2.4J and 5.4J significantly reduced creatine kinase levels only after the second application, whereas since the first application the dose of 8.4J was able to significantly increase the levels of the antioxidant enzyme superoxide dismutase and reduce the levels of creatine kinase and malondialdehyde, biomarkers of muscle damage and oxidative stress respectively[28].

In surgically induced muscle injury in the gastrocnemius muscle

of rats, the application of LLLT (785 nm; 75 mW; 0.07 cm^2; 12s; 0.9J) inhibited the inflammatory response and enhanced fibroblast proliferation, what accelerated the formation of scar tissue and stimulated the activation of satellite cells, thus contributing to the organization of the regenerated muscle fibers[6]. In an *in vitro* study, satellite cells arranged along isolated muscle fibers that received LILT (632.8 nm; 4.5 mW; 0.18 cm^2; 3s; 0.013J) in a single application, were activated and entered the cell cycle that leads them to the condition of new muscle fibers[26]. This dose may seem small, but it should be considered that LLLT was applied directly to the culture dish with no barrier between the laser beam and the irradiated cells. In rat gastrocnemius muscle, tissue resistance can weaken the radiant power of a laser beam from 60 mW to 20 mW after it crosses the skin and cause it to reach with only 5 mW the deeper muscle fibers[25].

The beneficial effects of LLLT (904 nm; 700 Hz; 15 mW; 0.2 cm^2) with irradiation times of 7; 20; 67 and 200s, and doses of 0.1; 0.3; 1 and 3J respectively, were also noted in the development of muscle fatigue and blood levels of lactate and creatine kinase when administered previously to a model of electrically induced tetanic contractions in rats. The doses of 1 and 3J were the only ones that significantly delayed muscle fatigue, and while all doses significantly reduced the lactate levels, only the dose of 3J did not significantly reduced the creatine kinase levels. Therefore the dose of 1J was the only one that showed a significant beneficial effect on all evaluated indexes[30]. The results achieved in this study are important since they reveal a preventive potential of LLLT in clinical practice.

Conclusion

Noting the correlation between the physiological events involved in the muscle injury recovery and the scientific evidence of LLLT effects available in the literature, it is possible to verify the therapeutic potential of LLLT at all phases of the muscle recovery process. While its anti-inflammatory and antioxidative properties have been shown to be helpful in reducing the deleterious effects of acute inflammation response, its bio-stimulant properties has proven to be extremely beneficial to the events involved in the repair phase. However, the wide variation observed in the parameters adopted for the application of LLLT in muscle injuries, makes it clear the need for future studies to determine which doses are most effective for achieving the best results.

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Received May 17, 2010
Accepted July 5, 2010