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Effect of Photo Biomodulation on Muscle Repair: a Literature Review

Efeito da Fotobiomodulação Sobre o Reparo Muscular: uma Revisão de Literatura

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Abstract

Muscle injuries are frequent, both in the practice of exercises and in the work environment, and after the injury, healing begins. The inflammatory phase of muscle healing is accompanied by an increase in the production of reactive oxygen species (ROS), and a reduction in the antioxidant activity of defense enzymes. This imbalance between both can generate oxidative stress, which can cause oxidative damage by directly affecting vital cellular constituents, such as lipids, proteins and DNA, in addition to interfering negatively in the muscle cells differentiation . Therefore, substances or therapies that stimulate antioxidant repair and defense are crucial to keep the levels of free radical production low, and to minimize factors that delay or prevent tissue recovery, among these therapies photo biomodulation has stood out. The objective of this literature review is to clarify the FBM effect on oxidative stress and muscle repair. Therefore, a search was carried out in the databases of Pubmed, Scielo, Lilacs and PEDro, using the keywords "Photo biomodulation", "low power laser", "muscle repair", "oxidative stress", and in English were "Photo biomodulation", "low level laser therapy", "muscle repair" and "oxidative stress". The texts that addressed the research topic, published between 2000 and 2020, were chosen. After analyzing the articles, it was possible to observe that photo biomodulation, despite presenting a great variety of parameters, moment of application and irradiation protocol found in the literature, shows beneficial results in the repair muscle and in the reduction of oxidative stress and fatigue markers.

Keywords: Low-Level Light Therapy. Oxidative Stress. Edema.

Resumo

Lesões musculares são frequentes, tanto na prática de exercícios como no ambiente de trabalho, sendo que após a lesão, inicia a cicatrização. A fase inflamatória da cicatrização muscular é acompanhada do aumento da produção de espécies reativas de oxigênio (ERO) e uma redução da atividade antioxidante das enzimas de defesa. Este desequilíbrio entre ambos pode gerar o estresse oxidativo, que leva a danos e atingi diretamente constituintes celulares vitais, como lipídios, proteínas e DNA, além de interferir negativamente na diferenciação das células musculares. Portanto, substâncias ou terapias que estimulem a reparação e a defesa antioxidante são cruciais para manter os níveis de produção de radicais livres baixos, e minimizar os fatores que atrasam ou impedem a recuperação do tecido, dentre estas terapias a fotobiomodulação tem se destacado. O objetivo da presente revisão de literatura é esclarecer o efeito da FBM sobre o estresse oxidativo e o reparo muscular. Sendo assim, realizou-se uma pesquisa nas bases de dados da Pubmed, Scielo, Lilacs e PEDro, utilizando as palavras-chave "Fotobiomodulação", "laser de baixa potência", "reparo muscular", "estresse oxidativo", e em inglês foram "photobiomodulation", "low level laser therapy", "muscle repair" e "oxidative stress". Foram escolhidos os textos que abordavam o tema da pesquisa, publicados entre 2000 e 2020. Analisando os artigos foi possível observar que a fotobiomodulação apesar de apresentar grande variedade de parâmetros, momento de aplicação e protocolo de irradiação encontrados na literatura, mostra resultados benéficos no reparo muscular e na diminuição de marcadores do estresse oxidativo e fadiga.

Palavras-chave: *Terapia com Luz de Baixa Intensidade. Estresse Oxidativo. Edema.*

1 Introduction

Muscle injuries are frequent in sports and work environment. More than 30% of the injuries observed in doctor's offices are related to the musculoskeletal system. Such lesions may occur through a variety of mechanisms, including those that arise through direct traumas (laceration or contusion), and those by indirect trauma (ischemia, loss of innervation, tension), but the general muscle repair process is similar in most cases[1].

Healing is one of the most complex biological events that results from the interaction between different tissue structures and a large number of cells that infiltrate, including neutrophils, macrophages, mast cells, and lymphocytes. This process triggers a series of events characterized by distinct stages, but interconnected, called inflammation, epithelization, deposition of connective tissue, and contraction, which involve the action of specific cells and numerous cytokines[2].

The inflammatory phase of muscle healing is accompanied by an increase in the production of reactive oxygen species (ROS) and nitrogen, and a reduction in the antioxidant activity of defense enzymes. This imbalance between pro-oxidants and antioxidants can generate oxidative and nitrative stress, which contribute to the activation of nuclear factor kappa B (NF-KB), which is a pleiotropic transcription factor, responsible for many changes in the expression of inflammatory process genes. Excessive production of these mediators can be harmful to muscle repair, which intensify inflammation and may inhibit the myoblasts differentiation, impairing the muscle tissue regeneration[3].

In addition, oxidative stress has been reported in numerous diseases such as diabetes mellitus, neurodegenerative disorders (such as Parkinson's, Alzheimer's, Multiple Sclerosis), cardiovascular diseases (such as atherosclerosis and hypertension), respiratory diseases (such as asthma), cataract development and rheumatoid arthritis. Studies have shown increased ROS markers of oxidative damage in blood and tissues of humans and animals during and after muscle damage. After muscle injury, oxidative stress could be increased due to several potential sites for the ROS generation in the traumatized muscle[(1)]. Due to the importance of this process, substances or therapies that stimulate antioxidant repair and defense are crucial to keep production levels of free radicals low, and to minimize factors that delay or prevent tissue recovery[2].

Among the therapies studied, photobiomodulation is highlighted, which uses a monochrome light in the lasers optical region, red or infrared, to treat several tissues in a non-destructive and thermic way, and the treatment is based on the light ability to change the cellular metabolism, particularly, due to the result of its absorption by mitochondria and C oxidase cytochrome[4].

Some laser properties characterize its applicability in therapies, such as: continuous or pulsed wave emission, intensity, monochromaticity, collimation or directionality. These properties are important for low-power therapy, which is based on excitation of endogenous chromophores in biological tissues that absorb visible (red) or invisible (infrared) radiation in doses of 1-10 J/cm², that do not cause tissues heating[5].

Photobiomodulation (FBM) applied before or after injury has shown positive and protective effects on muscle repair, including modulation of inflammatory process, angiogenesis, collagen fibers remodeling, as well as formation of new muscle fibers[4]. However, the parameters used in this therapy are still confusing and controversial in the literature. The objective of this literature review is to clarify the FBM effect on oxidative stress and muscle repair.

2 Development

2.1 Studies selection

Therefore, a search of scientific articles was carried out in the databases of Pubmed, Scielo, Lilacs and PEDro, using the keywords "Fotobiomodulação", "laser de baixa potência", "reparo muscular", "estresse oxidativo", and in English were "photobiomodulation", "low power laser", "muscle repair" and "oxidative stress". The texts that addressed directly the research topic, published between 2000 and 2020, were chosen.

2.2 Oxidative stress and muscle repair process

Muscle repair is very complex and involves several highly organized molecular and cellular processes. Immediately after the myofibers rupture, neutrophils and macrophages infiltrate the area of the lesion, producing proinflammatory cytokines and proteases responsible for the removal of necrotic tissue and subsequent propagation of the inflammatory response. These processes are clinically reflected by the formation of edema, local hematoma and a significant increase in serum levels of creatine kinase (CK), IL-1β and IL-6 cytokines and lactate dehydrogenase[3].

After injury, the muscular repair process begins and is divided into interdependent phases: degeneration and inflammation, regeneration, fibrosis/scars formation and remodeling[4].

The first phase, inflammatory, is accompanied by an increase in the ROS and nitrogen production and a reduction in the activity of antioxidant defense enzymes. This imbalance between pro-oxidants and antioxidants can generate oxidative and nitrative stress in the tissue that contributes to activating NF-κB, a pleiotropic transcription factor responsible for multiple changes in gene expression in the inflammatory process. These gene products include pro-inflammatory cytokines, growth factors, chemokines and adhesion molecules. Excessive production of these mediators may be harmful to muscle repair, as it intensifies inflammation and may inhibit the myoblasts differentiation, impairing the muscle tissue regeneration[3].

There is increasing evidence that ROS, such as free radicals and hydrogen peroxide (H_2O_2), is also involved in the pathophysiology of neurodegenerative diseases. One of the main culprits of oxidative modification, damage to macromolecules such as DNA and also oxidative stress is H_2O_2, produced during redox reactions. It could change the normal cellular functions and integrity. In fact, the level of oxidant/antioxidant is critical in neurodegeneration or neuroprotection[6].

In addition to post-injury muscle repair, it is found in the literature on post-exercise muscle recovery. It is known that the regular practice of physical activities is an important factor in health promotion, however, the frequent performance of high-intensity or exhaustive physical exercises may increase susceptibility to injuries, promote chronic fatigue and overtraining, partly due to the ROS high synthesis. Experimental evidence indicates that these compounds may be involved in the development of several pathophysiological processes such as aging, cancer, inflammatory diseases and atherosclerosis[7].

During the acute phase, there is the ROS release that at adequate levels in combination with growth factors and cytokines is important for the muscle repair process due to the redirection of the myogenic precursor cells (satellite cells) at the site of the lesion. However, high levels of ROS over a long period of time in the injured area can cause oxidative damage (secondary damages) by directly affecting vital cellular constituents, such as lipids, proteins and DNA, in addition to negatively interfering in the muscle cells differentiation[4].

Therefore, ROS can activate several signaling pathways that affect cell migration, cell cycle transition, cell survival, apoptosis and differentiation, crucial for tissue repair. At low to moderate levels, ROS stimulates healing and maintenance of muscle tissue, but if the ROS generation persists for a long time and at very high levels, it may delay tissue repair and even worsen injury[8].

2.3 Photo biomodulation Effect and oxidative stress and muscle repair

Photobiomodulation (FBM) was discovered almost 50 years ago by Endre Mester in Hungary. It was known for a long time as "low-power laser therapy," such as ruby laser (694 nm) and HeNe lasers (633 nm) being the first devices used. Recently, a consensus decision was made to use the terminology "FBM", since the term "low power" was very subjective. For a long time, the FBM mechanism of action was not clear, but in recent years there has been much progress in the elucidation of chromophores and signaling pathways[9].

Most of the initial work in this field was carried out with several types of lasers, and laser light was believed to have some special characteristics not possessed by light from other sources, such as sunlight, fluorescent or incandescent lamps, and now LEDs. However, all studies that were done comparing lasers to equivalent light sources with similar wavelength and power density in their emissions, did not essentially find any difference between them[9].

In the last decade, literature has reported an increasing interest in the application of FBM using different sources of light in diseases related to increased oxidative stress, but the mechanisms involved in this response remain obscure, mainly concerning the FBM effects on mitochondria, respiratory chain and on oxidative stress biomarkers [10].

FBM uses monochrome light in the optical region of red and infrared lasers to treat multiple tissues in a non-destructive and non-thermal manner. The treatment is based on the light capacity to change cellular metabolism, mainly as a result of absorbance by mitochondria and C oxidase cytochrome[4].

C oxidase cytochrome is the unit IV in the mitochondrial electron transport chain. It transfers one electron (from each of the four cytochrome C molecules) to a single oxygen molecule, producing two water molecules. At the same time, the four necessary protons are translocated through the mitochondrial membrane, producing a proton gradient that the adenosine triphosphate (ATP) enzyme synthase needs to synthesize ATP. Each of these metal centers can exist in an oxidized or reduced state, and they have different absorption spectra[9].

In addition to other special properties of laser light, which have led to its usefulness in many applications in therapy: continuous or pulsed wave emission, intensity, monochrome and collimation or directionality[5], as well as wavelengths, being considered red (600-700 nm) and infrared (770-1200 nm)[11].

Recently, blue and green wavelengths have also begun to be explored, but they have great problems with the depth of penetration. It is accepted that the penetration of light into the tissue is governed by the absorption and dispersion of the molecules and structures present in the tissue[9].

Among the various interventions used to prevent and treat exercise-induced muscle damage, FBM is an emerging approach. This intervention is indicated before exercise and/or training, and it has potential benefits in muscle tissue. Among many potentially responsible mechanisms por this event, increases in energy metabolism and ATP synthesis, stimulation of defenses against oxidative stress, and prevention or repair muscle damage may be the justification. As a result, it may accelerate post-exercise recovery and positively affect sports performance[12].

In addition, FBM changes the redox state in cells and may induce activation of intracellular signaling, increase the activation of redox sensitive transcription factors, and affect enzyme activation and the cell cycle progression, which are fundamental mechanisms involved in healing[10].

FBM not only reduces the harmful effects of H_2O_2, but also increases the antioxidants expression and reduces oxidative stress, and in addition there is an improvement in regeneration quality and recovery time[6]. Therefore, FBM applied before or after injury has shown positive and protective effects on muscle repair, including modulation of inflammatory process, angiogenesis, collagen fibers remodeling, as well as formation of new muscle fibers[4].

Several studies in the literature show beneficial effects of FBM on muscle recovery after exercise, favoring performance in physical activities and sports, as well as reducing oxidative stress indicated by markers such as CK and lactate levels.

According to the findings herein, different parameters of FBM can provide distinct effects on muscle tissue. When it comes to studies that used the laser in the red band, it was evidenced in this study that FBM has different effects on muscle level, and it is possible to detect an increase in maximum voluntary contraction, an increase in oxygen consumption, decrease in the percentage of blood lactate levels and fatigue markers[13-15].

In studies using infrared wavelength, only two studies have shown a decrease in peak strength and an increase in exhaustion and time to reach fatigue[16,17], another two studies have not shown a significant difference in strength measured with a digital dynamometer, or in pain and fatigue[18,19]. On the other hand, nine studies have shown significant results in increased muscle strength, increased oxygen consumption and longer time to reach exhaustion, decreasing fatigue markers[13-16,20-24].

Some studies also demonstrate that FBM applied before exercise can prevent muscle damage, increasing maximum voluntary contraction as well as improving oxygen consumption, increasing the time to reach exhaustion and decreasing CK activity, lactate levels and fatigue markers[13,14,16,21,23], as well as studies that applied FBM after exercise, also demonstrated a decrease in oxidative stress markers[22,24].

3 Conclusion

It can be concluded that FBM presents beneficial results in muscle repair and decreased markers of oxidative stress and fatigue, despite the wide variety of parameters applied in the literature, as well as the moments and protocols of application.

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