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REVIEW ARTICLE OPEN ACCESS

PHOTOBIOMODULATION APPLIED TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): A REVIEW

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ABSTRACT

Photobiomodulation is the use of visible and infrared light through light emitting diodes - LED without thermal and cytotoxic reactions.It was carried out a literature review with this studyto understand photobiomodulation applied to Chronic Obstructive Pulmonary Disease - COPD.It was carried out a survey in January 2023, in the SciELO, Lilacs, Pubmed, Medline and Google Scholar databases. With the descriptors “Low-level light therapy” AND “Chronic obstructive pulmonary disease” AND “Phototherapy” and in English “Low-level light therapy” AND “Pulmonary Disease, Chronic Obstructive” AND “Phototherapy”. It was selected 04 papers after applying the inclusion criteria. From the analysis of the data, it was possible to verify that 50% of the papers said that photobiomodulation improved the functional capacity of the muscles of the lower limbs in patients with COPD.In addition, 25% of the selected studies demonstrated improvement in pulmonary ventilatory mechanics and elastance, restoration of the balance between pro-inflammatory and anti-inflammatory cytokines, reduction in collagen deposition in the airways and decrease in interstitial tissue thickening. We conclude that photobiomodulation is an effective, low-cost, easy-to-adhesion and promising resource in the rehabilitation process of patients with COPD, for reversing the evolutionary processes of the disease and improving functionality.

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INTRODUCTION

The Chronic Obstructive Pulmonary Disease (COPD) is the third cause of death worldwide. In this sense, 90% of deaths from COPD occur in low-income countries, with an increase in the prevalence of mortality in recent decades. And, in Brazil, it affects 6 million people, where only 12% are diagnosed, of these 12%, only 18% receive treatment (Singh D *et al.,* 2019). Thereby, the COPD is a change in the airways that causes destruction of alveoli and adjacent vessels, limiting expiratory airflow due to a chronic and heterogeneous inflammatory process, causing physiological deterioration and damage to the pulmonary functional architecture (Mokmeli & Vetrici, 2020; Stockley *et al*., 2019; Zecha *et al*., 2016). Namely, COPD is more common in people over 50 years old and its main cause is associated with smoking, in addition to exposure to air pollution, frequent lower respiratory infections during childhood, occupational chemicals and dust (Singh D *et al*., 2019).

It's not only that, however, the COPD reached a morbidity rate of 40,051 cases, with 456,189 hospitalizations in Brazil from January 2018 to December 2022, equivalent to 7.6 hospitalizations per year, from January 2018 to December 2022. 2022, according to data from the Department of Informatics of the Unified Health System (DATASUS) (Brazil, 2023). As a result, the average hospital stay was 6.4 days and mortality were 8.78, which represents a burden on hospital services of BRL 489,319,197.26 in the sum of this entire period from January 2018 to December 2022, during hospital stay (Brazil, 2023). Still, COPD has no cure, but it has primary pharmacological treatment and non-pharmacological therapies as rehabilitative action measures, to promote better quality of life, control symptoms and reduce the risk of exacerbations (Singh D *et al.,* 2019). It's not only that, however the treatment of COPD starts with smoking cessation, cardiorespiratory physiotherapy, surgical and pharmacological treatment with bronchodilators such as salbutamol, fenoterol or ipratropium bromide, in more severe cases, continuous oxygen therapy (Brazil, 2021). In this sense, the light as a therapeutic resource has been used since the 19th century when, in 1978, low-level laser therapy was empirically used in respiratory tract diseases such as pneumonia, asthma and bronchitis (Mokmeli & Vetrici, 2020). In this sense, low-intensity laser therapy has a wavelength< 500 mW, ranging from 450-1100nm, is non-invasive, painless, easy to apply, safe, with little side effects, with no reports of serious adverse events in the literature, as in photobiomodulation (Chow *et al*., 2009). Therefore, photobiomodulation is a multidisciplinary resource applied in dentistry, nursing, sports medicine, and physiotherapy with the use of visible and infrared light through lightemitting diodes - LED without thermal and cytotoxic reactions (Freire *et al*., 2021; Leal Junior *et al*., 2009; Zecha *et al*., 2016). Having said that, among the benefits of applying in vivo photobiomodulation is increased local microcirculation, lymphatic drainage of the body, increased cellular metabolism and analgesia, in addition to the reduction of inflammatory processes, interleukin 1 and 6, cellular influx of neutrophils, tumor necrosis - TNF, oxidative stress, bleeding and edema(Chow *et al*., 2009; Mokmeli & Vetrici, 2020). Therefore, photobiomodulation is a non-invasive, safe, low-cost and highly effective resource for treating musculoskeletal and cardiovascular pathologies and, more recently, lung diseases such as asthma, bronchitis and COPD (Bian *et al*., 2022; Moraes *et al*., 2018; Oliveira *et al*., 2014; Zecha *et al*., 2016).

This way, there are no records in the literature of a protocol or guide for the therapeutic application of photobiomodulation in patients with COPD. Finally, how should the safe use of photobiomodulation be in patients with COPD?

Nevertheless, photobiomodulation is well applied in the performance of athletes before or after competition, generally applied in upper limbs - MMSS and lower limbs - MMII, increasing the potential of muscular work and reducing post-training fatigue. However, in diseases such as COPD, existing studies are aimed at finding the benefits of photobiomodulation, however without a defined therapeutic window. Therefore, the general objective of the current study was to carry out a systematic review of the literature to present the effects of photobiomodulation applied to COPD, modes and areas of application, parameters used, in addition to resources associated or not for the purpose of justifying this resource for therapeutic application in the conditions of patients diagnosed with COPD.

MATERIALSAND METHODS

The search terms used in this systematic review were obtained by consulting the Health Sciences Descriptors (decs.bvs.br). It was carried out a literature survey in January 2023, in the bibliographical research the SciELO, Lilacs, Pubmed, Medline and Google Scholar databases were used. It was used in the search for papers the following descriptors: “Low-Level Light Therapy” AND “Chronic obstructive pulmonary disease” AND “Phototherapy” and, in English, “Low-Level Light Therapy” AND “Pulmonary Disease, Chronic Obstructive” AND “Phototherapy” in all databases.

RESULTS

Thus, it was selected 04 papers and included according to the eligibility criteria as shown in Figure 1. The inclusion criteria werepapers in English and Portuguese, in the last five years, involving photobiomodulation in chronic obstructive pulmonary disease - COPD. Book chapters, event summaries, case reports, editorials, systematic reviews, meta-analyses, and opinion articles were also excluded.

DISCUSSION

The aim of this study was to carry out an integrative literature review to understand photobiomodulation applied to chronic obstructive pulmonary disease - COPD. In this sense, studies on the use of photobiomodulation point to a low-cost therapeutic option, without side effects and easy adherence by the patient. With great application in the conditioning of athletes, oncological rehabilitation, tissue regeneration and currently in lung diseases (de Souza *et al*., 2020; Ferraresi *et al*., 2016; Miranda *et al*., 2019; Moraes *et al*., 2018; Oliveira *et al*., 2014; Wei *et al*., 2020; Wiehe *et al*., 2019). This is because photobiomodulation does not require the use of inputs, and equipment maintenance is carried out with simple sterilization. The application is made in contact with the skin, without invasive measures and pain. In addition, the infiltrated light does not produce heat in the tissue, and these factors increase adherence to treatment, an example of which is the use in patients with COPD (Evan Steele, 2021; Freire *et al*., 2021; Sayed *et al*., 2018). Then, photobiomodulation has become a therapeutic possibility for repairing lung tissue damage, despite not yet having a definition of a conductive therapeutic window (Lin *et al*., 2010; Peron *et al*., 2015). This is because studies in patients with pneumatic diseases are still recent. An example of this is that the World Association for Photobiomodulation Therapy - WALT does not have recommendations or guidelines for COPD (WALT, 2010).

However, doses between 1J/cm² and 5J/cm² have been shown to be efficient in reducing pro-inflammatory cells in the bronchoalveolar fluid - BAF, reversing lung tissue necrosis and cell apoptosis, in addition to regulating reactive oxygen species (ROS) and increase in the synthesis of adenosine triphosphate – mitochondrial ATP(Soares, 2021). This phenomenon can be explained, through the interaction of light in contact with the cell, which dissociates nitric oxide- (ON) in mitochondria under stress, preserving oxygen, and maintaining significant amount of ATP (Sayed *et al*., 2018). Thereupon, the control of oxidative stress decreases the recruitment of neutrophils, and the interleukins responsible for inflammatory signaling are not released. Reversal of necrosis and apoptosis further decreases this inflammatory potential (Rufino *et al*., 2006). Thus, the regulation of ROS becomes a consequence of the cascade of reactions found and provides other benefits such as: greater control of capillary permeability, less mucus production and a decrease in episodes of bronchoconstriction (Rufino *et al*., 2006). In addition, another study demonstrated an improvement in the functional capacity of patients with COPD by increasing performance in the 6MWT through a single application of photobiomodulation in the respiratory muscles of patients with COPD (de Souza *et al*., 2020).

This phenomenon must occur when light absorbed at the cellular level generates a chain of reactions involving improvement in muscle perfusion, arteriolar vasodilation, and improvement in blood supply through cytochrome C oxidase (Miranda *et al*., 2014). In this way, there is an increase in mitochondrial metabolism, muscle glycogen synthesis, muscle cell proliferation, tissue oxygenation and nutrition by increasing circulation, so the feeling of fatigue becomes less and exercise tolerance greater (Ferraresi *et al*., 2016). E, also, by reducing the lactate threshold and muscle acidosis present in fatigued muscles, these metabolites disrupt the contractile process and inhibit ATP production. Photobiomodulation reverses this situation and improves the performance of high-performance activities and reduces perceived fatigue (Pinto *et al*., 2016). In this sense, through the direct application of photobiomodulation in the lower muscles (MMII), regardless of association with another therapy, an improvement in functional capacity was observed through the 6MWT and reduction of fatigue in the lower limbs in patients with COPD (Ferraresi *et al*., 2016; Miranda *et al*., 2019). This is because the modulation of mitochondrial activity is the main mechanism for photobiomodulation through the improvement of muscle metabolism. It was possible to observe a reduction in the dyspnea scale and an increase in muscle performance. Therefore, tolerance for walking on a longer route became less fatiguing (Miranda *et al*., 2019). So, in view of the studies mentioned so far, the modulation of cellular metabolism also produces a satisfactory response in the fatigue of patients with COPD and other pathological conditions, corroborating other findings in the literature (Alves *et al*., 2019). In this sense, photobiomodulation applied directly to the lung and airways demonstrated a reduction in alveolar enlargement, collagen deposition in the airways, an increase in elastance and lung mechanics, in addition to controlling inflammation (Moraes *et al*., 2018).

Tabela 1. Demonstrativo dos artigos que formam a Revisão

N	Data	Título	Autores	Periódico	Objetivos	Resultados
1	2021	Photobiomodulation therapy regulates the production of reactive oxygen species (ROS) in an experimental model of chronic obstructive pulmonary disease (COPD)	Stephanie Souza Soares, Ana Paula Ligeiro de Oliveira	Universidade Nove de Julho UNINOVE	To evaluate whether photobiomodulation therapy regulates pulmonary inflammation via reactive oxygen species (ROS) in an experimental model of chronic obstructive pulmonary disease (COPD) induced by cigarette smoke extract.	Photobiomodulation is effective in the pulmonary inflammatory response in an experimental model of COPD. Lower doses of the laser have an anti-inflammatory effect, and in part, involve the regulation of ROS.
2	2019	Acute effects of photobiomodulation therapy applied to respiratory muscles of chronic obstructive pulmonary disease patients: a double-blind, randomized, placebo-controlled crossover trial	Guilherme Henrique Martins de Souza, Cleber Ferraresi, Marlene Aparecida Moreno, Bruna Varanda Pessoa, Ana Paula Moraes Damiani, Vinicius Gasparotto Filho, Giovanny Viegas dos Santos, Antonio Roberto Zamunér	Lasers in Medical Science	To apply photo biomodulation to the respiratory muscles of patients with COPD to evaluate the effects on functional capacity, thoracoabdominal mobility, and respiratorymuscle strength.	Photo biomodulation in respiratory muscles was effective in improving functional capacity, but didnot identify the effectiveness of photo biomodulation in thoracoabdominal mobility and respiratory muscle strength of patients with COPD, evaluated by the 6-Minute Walk Test (6MWT).
3	2018	Acute effects of photobiomodulation therapy (PBMT) combining laser diodes, light-emitting diodes, and magnetic field in exercise capacity assessed by 6MST in patients with COPD: a crossover, randomized, and triple-blinded clinical trial	Eduardo Foschini Miranda, Welton Alves Diniz, Marcos Vinicius Nogueira Gomes, Marcelo Ferreira Duarte de Oliveira, Paulo de Tarso Camillo de Carvalho, Ernesto Cesar Pinto Leal-Junior	Lasers in Medical Science	To apply the combined photobiomodulation of Led, lasers and magnetic field in patients with COPD evaluating effects on muscle performance, exercise tolerance and metabolic variables during the (6MWT	The combined photobiomodulation of Led, lasers and magneticfield in patients with COPD contributedto the increase of steps in the 6MWT, with improvement of the muscular performance of the LowerLimbs–LLL Land greater exercisetolerance inpatients with COPD. Low-intensity lasertherapyhas shown a reduction in pulmonary changes, especially in the reduction of inflammatorycytokines, leukocytes in the bronchoalveolarl avage fluid-balf, collagendeposition in theair ways, reduction in the expression of purinergic recept or and emphysema. It also showed increase dventilatory mechanics and reestablishment of anti-inflammatorytoxins.
4	2018	Low-Level Laser Therapy Reduces Lung Inflammation in an Experimental Model of Chronic Obstructive Pulmonary Disease Involving P2X7 Receptor	Gabriel da Cunha Moraes, Luana Beatriz Vitoretti, Auriléia Aparecida de Brito, Cintia Estefano Alves, Nicole Cristine Rigonato de Oliveira, Alana dos Santos Dias, Yves Silva Teles Matos, Manoel Carneiro Oliveira-Junior, Luis Vicente Franco Oliveira, Renata Kelly da Palma, Larissa Carbonera Candeo, Adriana Lino dos Santos Franco, Anna Carolina Ratto Tempestine Horliana, João Antonio Gimenes Júnior, Flavio Aimbire, Rodolfo Paula Vieira, Ana Paula Ligeiro de Oliveira	Oxidative Medicine and Cellular Longevity	To investigate whether low-intensity laser therapy reduces lung changes in patients with COPD.	

This can be explained by means of angiogenesis, thickening of the basement membrane, increase in elastic fibers, production of mucus and collagen in adequate quantity, present in the remodeling process of the upper airways (UAW) (Constantino, Mello Jr, 2009). Namely, other studies corroborate these findings and highlight that red light in the range of 600nm to 700nm and infrared light from 700nm to 1000nm has the potential to reduce pulmonary fibrosis (Brochetti *et al*., 2017; de Brito *et al*., 2020; Miranda *et al*., 2014). Thus, it is possible to observe improvement in the maintenance of airway integrity and purinergic gradation, through the modulation mechanism. With improved elastance and this reduces the forced work of breathing in patients with COPD (de Brito *et al*., 2020; Miranda *et al*., 2014). For example, a study treating fibrotic mice showed that LED reduces static and dynamic elastance of the lungs, as well as collagen and interstitial tissue thickening (Moraes *et al*., 2018). Thus, in experimental pulmonary fibrosis, photobiomodulation attenuates lung inflammation, remodels the airways, restores the balance between pro-inflammatory and anti-inflammatory cytokines, in addition to inhibiting pro-inflammatory cytokines and fibroblasts (Brochetti *et al*., 2017; de Brito *et al*., 2020; Enwemeka *et al*., 2020). Despite this, therapeutic windows and areas of application are not homogeneous in patients with COPD. It was evaluated respiratory muscles, quadriceps, and lung lobes, and the reduction in the sensation or perception of fatigue was unanimous in these studies (de Souza *et al*., 2020; Miranda *et al*., 2014, 2019; Moraes *et al*., 2018; Soares, 2021).

Thus, therapeutic applications take place before physical activity or after exercise to accelerate the recovery of inflammatory processes caused by the practice of high-performance activities or in cases of chronic fatigue (Kuan *et al*., 2019; Leal Junior *et al*., 2009; Luo *et al*., 2022). And another important fact related to the therapeutic application is the time, which varies from 0.30 seconds to 0.45 seconds per microarea, which may be an initial range for the time variable in the therapeutic window in patients with COPD (Ferraresi *et al*., 2016). On the other hand, applications in athletes or so-called healthy individuals happen for up to 05 minutes, at least 01 hour before sports practice, with a similar form of application (Ferraresi *et al*., 2016; Leal Junior *et al*., 2009). In this sense, the form of application was mostly carried out directly in the area under analysis, in continuous mode. Despite the few studies in populations with COPD, this practice is justified by the evidence shown regarding the positioning of the equipment and with promising results in the studied populations (Bian *et al*., 2022; Brochetti *et al*., 2017; de Brito *et al*., 2020; de Souza *et al*., 2020; Enwemeka *et al*., 2020; Kuan *et al*., 2019; Leal Junior *et al*., 2009; Luo *et al*., 2022; Miranda *et al*., 2014, 2019; Moraes *et al*., 2018; Peron *et al*., 2015). However, there was no report on the influence between equipment variability and the impact directly on the result, since different equipment demonstrated a good therapeutic outcome, regardless of the populations studied (Brochetti *et al*., 2017; de Brito *et al*., 2020; de Souza *et al*., 2020; Enwemeka *et al*., 2020; Evan Steele, 2021; Leal Junior *et al*., 2009; Miranda *et al*., 2014 , 2019; Moraes *et al*., 2018; Oliveira *et al*., 2014; Peron *et al*., 2015; Sayed *et al*., 2018). The reports corroborate each other regarding the domain of parameters already established in the literature, although there is no specific definition for the therapeutic window in COPD (Brochetti *et al*., 2017; de Brito *et al*., 2020; de Souza *et al*., 2020; Evan Steele, 2021; Leal Junior *et al*., 2009; Miranda *et al*., 2014, 2019; Moraes *et al*., 2018). And a frequency between sessions was also not observed. COPD-related protocols were made up of unique applications. What can limit outcomes. Because it is a subject little explored scientifically, randomized trials involving humans are still little reported in the literature, as well as studies involving animals in their samples.

CONCLUSION

The aim of this study was to perform an integrative literature review to understand photobiomodulation applied to chronic obstructive pulmonary disease - COPD. Therefore, it was demonstrated that the use of photobiomodulation is an effective, low-cost resource, without side effects, easy to adhere to because it is painless and non-invasive. Its use is wide in sports practice in the conditioning of athletes. In the clinical environment, the rehabilitation of the most different pathologies is directed, including lung diseases. Having said that, in the treatment of COPD it has been shown to be effective in improving functional capacity, increasing isometric resistance and exercise tolerance, reducing fatigue, controlling inflammatory processes by inhibiting pro-inflammatory toxins and fibroblasts, in addition to acting by restoring anti- inflammatory toxins. As well as reducing alveolar enlargement and collagen deposition in the airways, contributing to its remodeling process. Improvement of lung elastance, ventilatory mechanics and consequently exercise tolerance by reducing the feeling of fatigue. In this way, it was also demonstrated that the application of the therapy happened before the beginning of the exercises. Sessions 1 to 3 times a week. With an average duration of 0.30 to 0.40 seconds per micro area each application, directly in contact with the skin, and use of red light in the range of 600nm to 700nm and infrared from 700nm to 1000nm. Thus, the areas of application that showed better results were the quadriceps, when compared to the respiratory muscles. There was no homogeneity regarding the equipment, but all showed promising results without harm to the patient. In this sense, although the current literature is still scarce on the subject, we can conclude that photobiomodulation is an effective, low-cost, easy-to-adhere and promising resource in the functional rehabilitation process of patients with COPD. Some questions still need to be answered, such as the frequency of application and the intervals between them. Compare the effects of parameter variations to define the therapeutic window applied to the pathology. In addition to studies involving a more significant sample number.

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