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Comparative study of the effectiveness of ozone therapy and laser photobiomulation upon experimental wound repair: systematic review

Estudo comparativo da eficácia da terapia com ozônio e fotobiomodulação a laser no reparo experimental de feridas: revisão sistemática

Estudio comparativo de la efectividad de la ozonoterapia y la fotobiomodulación láser en la reparación experimental de heridas: revisión sistemática

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Abstract
Laser photobiomodulation and ozone therapy are therapeutic possibilities for antimicrobial control and biomodulation of tissue repair. This study aimed to compare the effect of laser photobiomodulation with that of ozone gas in wound healing of experimental lesions on animal's tissues. It was a systematic literature review, which aimed to search for articles of the animal model experimental study according the PRISMA guidelines. The search was made through the electronic articles indexed in the databases: PubMed, BVSalud, Cochrane, Scielo and Google Scholar, based on the DeCS/MeSH descriptors in English and Portuguese. The sample included studies from 2013 to 2020 and methodological quality was assessed using the ARRIVE guideline. A total of 329 of records indentified through database searching. Five studies were selected for the present systematic review according to the inclusion and exclusion criteria outlined for the research. All studies performed histological analysis of the treated tissue sections. Ozone therapy and laser showed a significant difference in favor of repair in different tissues when compared to the findings of the control groups in all studies. When compared to each other, ozone showed superiority over laser in two of the five studies, in addition to two studies having similar results between these two therapies. Regarding the ARRIVE guideline, in the most studies, the meeting criteria was high, with good methodological quality. Most studies highlighted the lack of uniformity in the therapy protocol as the greatest difficulty encountered, although they were unanimous in stating that laser photobiomodulation and ozone therapy contributed to the improvement of the healing pattern.
Keywords: Healing; Ozone; Low power laser therapy.

Resumo
A fotobiomodulação laser e a terapia com ozônio são possibilidades terapêuticas para controle antimicrobiano e biomodulação do reparo tecidual. Este estudo teve como objetivo comparar o efeito da fotobiomodulação laser com o

gás ozônio na cicatrização de lesões em tecidos de animais. Tratou-se de uma revisão sistemática que buscou estudos experimentais em modelo animal de acordo com os parâmetros PRISMA. A busca foi feita por meio de artigos indexados nas plataformas: PubMed, BVSalud, Cochrane, Scielo e Google Scholar, com descritores DeCS/MeSH, em inglês e português. A amostra incluiu estudos entre 2013-2020 e a qualidade metodológica foi avaliada através do guia ARRIVE. Um total de 329 registros foram identificados por meio de busca nas plataformas. Cinco estudos foram selecionados para o presente trabalho de acordo com os critérios de inclusão e exclusão delineados. Todos os trabalhos realizaram análise histológica dos tecidos tratados. A ozonioterapia e o laser mostraram diferença significativa a favor do reparo em diferentes tecidos quando comparados aos achados dos grupos controle em todos os estudos. Quando comparados entre si, o ozônio demostrou superioridade em relação ao laser em dois dos cinco estudos, além de dois trabalhos terem resultados semelhantes entre essas duas terapias. Em relação à diretriz ARRIVE, na maioria dos estudos os critério foram atendidos, o que confere uma boa qualidade metodológica. A maioria dos estudos destacou a falta de uniformidade nos protocolos, embora tenham sido unânimes em afirmar que a fotobiomodulação laser e a ozonoterapia contribuíram para a melhora do padrão cicatricial.
Palavras-chave: Cicatrização; Ozônio; Terapia de luz de baixa intensidade.

Resumen

La fotobiomodulación láser y la ozonoterapia son posibilidades terapéuticas para el control antimicrobiano y la biomodulación de la reparación. Este estudio tuvo como objetivo comparar el efecto de la fotobiomodulación láser con el del gas ozono en la cicatrización de heridas de lesiones experimentales en tejidos animales. Se trató de una revisión sistemática, que tuvo como objetivo la búsqueda de artículos del estudio animal según las guías PRISMA. La búsqueda se realizó através de los artículos indexados en las bases: PubMed, BVSalud, Cochrane, Scielo y Google Scholar, con descriptores DeCS/MeSH en inglés y portugués. La muestra incluyó estudios de 2013-2020 y la calidad metodológica se evaluó mediante la guía ARRIVE. Un total de 329 registros identificados a través de la búsqueda. Se seleccionaron cinco estudios para lo presente trabajo según los criterios de inclusión y exclusión. Todos los estudios realizaron análisis histológicos de tejido tratadas. La ozonioterapia y el láser muestran diferencias significativas que favorecen la reparación en diferentes tecidos cuando se comparan entre los dolores de dos grupos y el control de todos los estudios. Quando comparados entre si, o ozônio demuestra superioridade em em dois dos cinco estudos, y dois trabajos presentados resultados similares entre ensayos duas terapias. En cuanto a la guía ARRIVE, en la mayoría de los estudios el criterio de cumplimiento fue alto, con buena calidad metodológica. La mayoría destacó la falta de uniformidad en el protocolo de terapia la mayor dificultad encontrada, aunque fueron estudios específicos.
Palabras clave: Cicatrizácion de heridas; Ozono; Terapia de luz de bajo nivel.

1. Introduction

Wound repair is a complex biological process where the organism seeks to regenerate damaged tissues with your anatomical and functional integrity. This process may be influenced by the type of the injury, extent of damage, and properties of the tissue involved. Sometimes, the environmental conditions can impact the tissue repair, because the lesion contributes to infection development due to possible microbial species that exists in the tissue (Zhang et al., 2020).

The search for therapies that promote wound repair is mandatory. Currently, laser and ozone therapy are therapeutic possibilities in several health areas, especially for antimicrobial control and tissue repair (Silva et al., 2013; Bayer et al., 2017). Laser photobiomodulation, also called low-intensity laser therapy or laser therapy, promotes biological effects that can be classified as short and long term. The immediate effect includes an increase in mitochondrial ATP production, and in the long run, an increase in cell biosynthesis processes. In the proliferative phase of healing, this therapeutic modality is capable of stimulating neoangiogenesis, and this biological event is crucial for the supply of tissue nutrients and activation of pro-angiogenic factors, such as the vascular endothelial growth factor (VEGF), which results in the formation of new capillaries (Fortuna et al., 2017). It is believed that the mechanism of action of the laser involves the absorption of photons with identical wavelengths, by photoreceptors, such as the enzyme cytochrome C oxidase, to directly interfere in the synthesis of ATP through the acceleration of the electron transport chain (Freitas & Hamblin, 2016). Laser positively impacts the modulation of tissue repair as it contributes to the increase and improvement in the organizational pattern of collagen fibers. Also, this therapy stimulates the biosynthesis of important growth factors and the proliferation of fibroblasts (Isler et al., 2018).

Ozone is a gas present in the atmosphere, composed of three oxygen atoms that exerts a strong oxidizing action. It contains a variable molecular structure of high energy at normal temperature and is decomposed quickly and spontaneously into O_2 and an oxygen atom (Schulz, 1988). During this process, called ozonolysis, there is the formation of highly unstable reactive oxygen species. The antimicrobial effect results from the interaction of these radicals with unsaturated fatty acids and proteins in the cytoplasmic membrane of bacterial cells, which causes the reduction of enzymatic activity and interrupts the respiratory function of these microorganisms. This action is nonspecific and selective for microbial cells since they do not have an antioxidant system. Ozone has a therapeutic action in tissue repair by activating the mechanisms of protein synthesis, increasing the number of ribosomes and mitochondria in cells. These changes at the cellular level explain the increase in the functional activity and the potential for tissue and organ regeneration modulated by this therapy (Grootveld, 2004; Bocci, 2006).

Given the lack of consensus on which therapy is most effective in tissue repair, the objective of this systematic review was to comparatively evaluate the effectiveness of modulatory therapies, laser photobiomodulation, and ozone therapy, in the tissue repair microenvironment in controlled animal experimental studies.

2. Methodology

2.1 Eligibility criteria, search strategies and methodological quality

It was a systematic literature review carried out in February to March 2020, which aimed to search for articles of the animal model experimental study according the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyzes) for compiling and selecting studies, which answered the following central question: *Which modulatory therapy is most effective in wound healing, laser photobiomodulation or ozone therapy?* To answer this question, a search was carried out in the databases: PubMed, BVSalud, Cochrane, Scielo and Google Scholar.

As a search strategy, the following descriptors of the virtual health library (DeCS) were used in english: “healing”, “ozone”, “laser”, “low power laser therapy”, “laser photobiomodulation”; and their English counterparts: "wound healing", "ozone", "low-level laser therapy (LLLT), "laser photobiomodulation" and Portuguese: “cicatrização de feridas”, “ozônio”, “terapia de luz de baixa intensidade”, “fotobiomodulação a laser”; conjugated through the Boolean expression AND.

The anagram PICO was used, in which the population included studies that evaluated tests with animals and the intervention included laser photobiomodulation and ozone, used in the same study. Control was represented by experimental groups that did not receive treatment and for the outcome, the effects of these therapies on tissue repair were considered.

To maximize the evaluation, the ARRIVE (Animal Research: Reporting In Vivo Experiments) guideline was used, which is based on guiding essential information in animal studies in order to make the study reproducible, orderly, transparent, and accurate.

2.2 Exclusion and inclusion criteria

The criteria for selecting the articles included experimental studies carried out on animals, published between the years 2013 to 2020, and that consisted of comparative tests made with laser and ozone photobiomodulation. Studies that performed tests with humans or in vitro, editorials, letters to the editor and literature reviews, as well as clinical case reports, were not included. Studies without an abstract in the databases, monographs, dissertations, and theses were also excluded, because according to the scale of evidence in the Cochrane Manual for Systematic Reviews of Interventions, these modalities provide a low level of scientific evidence (Higgins & Green, 2011).

2.3 Article selection and data extraction

All selected articles were tabulated with Microsoft Word (version 2018). The articles were selected based on the title, abstract, and full text of the article based on previously established criteria. Two examiners (TOSA and CBSC) independently performed the selection in the databases. In case of disagreement between them, a third author (ARAPM) would have been called.

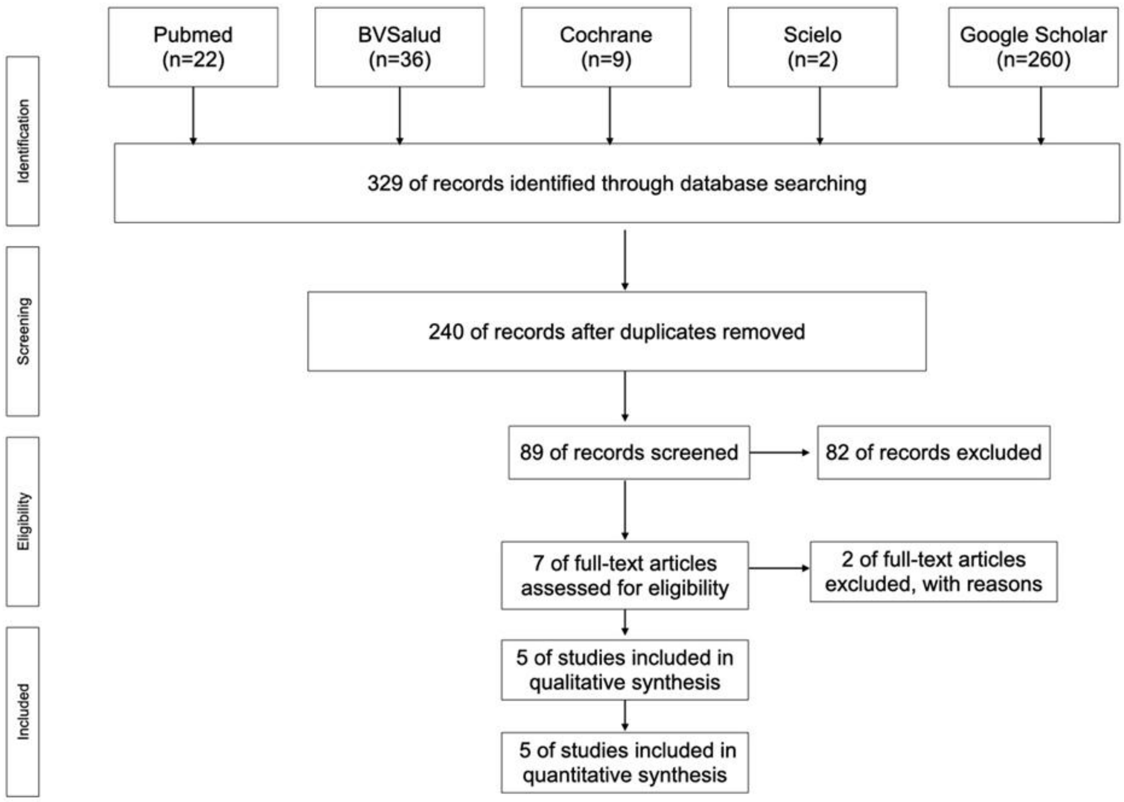
Data extraction was performed individually by searching for the following variables for each study: main author of the article; population (total sample (n) and description of the sample); intervention of the study (characteristics of ozone therapy and laser photobiomodulation); control, and main results. A descriptive analysis of the studies was made.

3. Results

The initial search strategy resulted in the selection of 22 articles taken from Pubmed, 36 from BVSalud, 9 from Cochrane, 2 from Scielo, and 260 from Google Scholar, totaling 329 articles. Two hundred and forty manuscripts were eliminated due to duplication. After reading the sample titles, 82 manuscripts were discarded, resulting in 7 selected articles. After the selective reading of the abstracts, 1 article was eliminated, and, after reading the full article, another study was eliminated because it did not meet the proposed theme. Thus, 5 articles met the inclusion criteria outlined for this systematic review (Alan et al., 2015; Bayer et al., 2017; Kazancioglu, Ezirganli & Aydin, 2013; Yucesoy et al., 2017; Yuca et al., 2020) (Figure 1).

Among the 5 cataloged studies, the inclusion of 2 different species of rats was observed. Four studies used Wistar and 1, animals of the Sprague-Dawley lineage. There was a uniformity regarding the sex of the animals, because in all the studies only male rats were used, which had a weight varying between approximately 200 to 300g. On average, the experimental groups in each study included 8 to 12 animals. In the 5 studies, a total of 127 rats were used. The study developed by Alan et al. (2015) used 36 rats allocated in 3 groups with 12 each; Bayer et al. (2017) used 24 rats allocated in 3 groups of 8 animals; Kazancioglu et al. (2013) designed a study with 30 rats designated in 3 groups containing 10 animals in each; Yucesoy et al. (2017) used 27 rats, with 9 allocated to each group and Yuca et al. (2020), 30 rats divided into 3 groups of 10 animals (Table 1).

Figure 1 - Flowchart of article selection through the different stages of the systematic review (PRISMA).



Search period: February to March 2020. Source: Author's data.

Table 1 - Characteristics of selected articles and main results. Search period: February to March 2020.

Author Year	*Population*	*Intervention: therapies*	*Control*	*Results*	*Guideline ARRIVE*
Alan et al. (2015)	36 male Wistar mice: Laser group (n=12), Ozone group (n=12), Control group (n=12).	Compare the effects of infrared laser (810 nm, 0.3W, 12 J/cm², 3 times a week, 28 days) and ozone gas, performed by topical application at 80% in wounds on the rat femurs for 30 seconds through a probe, filled with nano-hydroxyapatite.	Did not receive treatment.	The laser group had a lower bone formation index and a higher number of osteocalcin-positive cells, present in the connective tissue and on the bone surface, after 4 weeks. However, after 8 weeks, the laser group exhibited greater osteogenesis and the presence of osteocalcin in the bone marrow. The ozone group exhibited greater bone formation ($p>0.05$) after 4 weeks and greater expression of osteocalcin-positive cells after 8 weeks ($p<0.05$).	Absolute value: 16/20 80% meeting the criteria.
Bayer et al. (2017)	24 Sprague-Dawley mice. Laser group (n=8), Ozone group (n=8), Control group (n=8).	Compare the effects of laser and ozone therapy on mucositis induced by 5-FU (intraperitoneal, 100mg/kg on the 1st day and 65mg/kg on the 3th day). After the wound was induced, the laser group (940 nm, 7 and 14 J/cm²) received the application for 20 seconds and 5 days. The ozone group received 80% ozone gas, in the ulcerated area, for 120 seconds, for 5 days.	Did not receive treatment.	The laser group obtained an increase in PDGF-BB ($p<0.0001$). Although the ozone group stimulated the expression of bFGF, the laser group showed more significant results ($p=0.0002$).	Absolute value: 18/20 90% meeting the criteria.
Kazancioglu, Ezirganli & Aydin (2013)	30 Wistar mice. Laser group (n=10), Ozone group (n=10), Control group (n=10).	A bone defect of 5 mm in diameter was created in the calvaria of the rats, subsequently filled with a synthetic graft. The laser group (4J/cm², 808 nm, 120 seconds, 3 times a week, 14 days, was compared to the ozone group that received 80% ozone gas (120 seconds, 3 times a week, 14 days).	Did not receive treatment.	Histomorphometric analyzes showed that in the laser and ozone groups, there was greater bone neoformation than in the Control group ($p<0.05$). In the ozone group, the total new bone areas were greater compared to the laser group ($p<0.05$).	Absolute value: 15/20 75% meeting the criteria.

Yucesoy et al. (2017)	27 Wistar mice. Laser group (n=9), Ozone group (n=9), Control group (n=9).	Dissection and suture of the mental nerve were performed in 27 rats. One group received laser (618 nm, 20 mW/cm², 6 J/cm²) in the proximal and distal parts of the suture. Therapy was performed for 5 minutes daily for 21 days. Another group received treatment with ozone administered once every 3 days for 21 days, in a concentration of 75% for 60 seconds through an oral tube.	Did not receive treatment.	The number of Schwan cells was higher in the groups that received ozone and laser compared to the control group. A greater number of Schwan cells were obtained in the proximal segment (p> 0.05) compared to the distal lesion segment (p <0.05) in the treated groups, about the control.	Absolute value: 11/20 55% meeting the criteria.
Yuca et al. (2020)	30 Wistar mice. Control group (n=10), Laser group (n=10), Ozone group (n= 10).	Comparison of laser therapy (850nm, 100 mW/ cm^2, 4J/cm², over 21 consecutive days) and ozone therapy, through an insufflation in the peritoneum of a gas mixture of ozone and oxygen with a dose of 2 mL (80 µm/mL) for 21 days (once every 2 days), for the treatment of facial nerve damage in rats, assessed by histomorphometric analysis.	Did not receive treatment.	The ozone showed statistically significant results after facial nerve injury compared to laser and control in terms of nerve fiber branching (p=0.003), nerve fiber diameters (p=0.039), areas of nerve fibers (p=0.04) and numbers of axons (p=0.032). Although the laser group revealed a better healing pattern than the control group, the result was not statistically significant in terms of nerve fiber branching (p=0.680), nerve fiber diameters (p=0.742), areas nerve fibers (p=0.704) and axon numbers (p=0.758).	Absolute value: 13/20 65% meeting the criteria.

nm: nanometers; J: jaules; W: Watts; 5-FU: 5-fluorouracil; mW: micro Watts; PDGF-BB: Platelet-derived growth factor; bFGF: basic fibroblast growth factor; µm: micrometer. Source: Author's data.

Regarding laser therapy, the devices exhibited wavelengths ranging from 618nm to 940nm. Dosimetry also varied between 4 and 12 J/cm^2. Two studies opted for the clinical protocol for applying laser photobiomodulation on alternate days (Alan et al., 2015; Kazancioglu et al., 2013) and three, on consecutive days (Bayer et al., 2017; Yucesoy et al., 2017; Yuca et al., 2020).

All experimental groups that were treated with ozone therapy used this agent as a gas. However, the mode of application differed among studies. In three investigations, the administration occurred via perilesional (Alan et al., 2015; Kazancioglu et al., 2013). In the research carried out by Yucesoy et al. (2017) ozone gas was administered with the aid of an oral probe and Yuca et al. (2020) used the gas intraperitoneally. The concentration of ozone gas used was 75% in only one study (Yucesoy et al., 2017) and 80%, in the other manuscripts (Alan et al., 2015; Kazancioglu et al., 2013; Bayer et al., 2017; Yuca et al., 2020).

The use of biomodulatory therapies showed significant differences in favor of the repair in different tissues when compared to the findings of the Control groups in all studies (Alan et al., 2015; Bayer et al., 2017; Kazancioglu et al., 2013; Yucesoy et al., 2017; Yuca et al., 2020). When compared to each other, ozone showed superiority over laser in two of the five studies (Kazancioglu et al., 2013; Yuca et al., 2020), in addition to two studies having similar results between these two therapies (Alan et al., 2015; Yucesoy et al., 2017). Only one study showed the superiority of laser photobiomodulation (Bayer et al., 2017).

Regarding the ARRIVE guideline, notably, in the most studies (Alan et al., 2015; Kazancioglu et al., 2013; Bayer et al., 2017), the meeting criteria was high, with 80%, 90% and 75%, respectively. A little limitation in the studies of Yucesoy et al. (2017) and Yuca et al. (2020) were found, with 55% and 65% of meeting criteria, respectively. Table 1 shows the ARRIVE strategy.

4. Discussion

This systematic review described five experimental studies that evaluated the impact of ozone and laser photobiomodulation on repair in different experimental models of healing. All the modulatory therapies demonstrated in the studies had exhibited potential efficacy on the varied types of tissues studied when compared to Control groups. It is also noticed that older studies have a greater diversity of protocols, while more recent studies have sought to adopt consensus about methodological aspects. Given the current trend towards standardization of protocols, the authors of this systematic review opted for the selection of studies published in the last 8 years.

It was observed a variation in some parameters of the therapies used, such as the wavelength of lasers and the concentration of ozone gas. Alan et al. (2015) used laser photobiomodulation with a wavelength in the red band (810nm), fluency of 12 J/cm², three times a week, for four weeks. The authors compared laser photobiomodulation with the application of 80% ozone gas for 30 seconds and observed that, in a longer period, there was a greater formation of bone tissue in the laser group, but with a higher concentration of cells that react to osteocalcin in the ozone group. Bayer et al. (2017) compared the 940 nm laser with different fluences for 5 days and treatment with 80% ozone gas, 120 seconds per day, for 5 days, on the oral mucosa of rats with induced oral mucositis and reported better results with the photobiomodulation. However, the authors highlighted the loss of animals in the control group due to malnutrition, resulting from the experimental model of mucositis induction. But still, the two therapies had positive local and systemic effects on the mucous of rats.

Kazancioglu et al., (2013) used laser with a wavelength of 808 nm, with fluency of 4 J/cm² every 3 days for 15 days and in another group, applied 80% ozone for 120 seconds with the same periodicity. The authors obtained similar results for both groups regarding the formation of bone tissue, but in the ozone group, the total new bone areas were greater compared to the laser group. Yucesoy et al. (2017) tested the red laser (680nm) with 6 J/cm² of fluency, for 5 minutes daily for 21 days and ozone gas, in a concentration of 75% for 60 seconds, once every 3 days, for 21 days. In comparison to the control group, the treated groups showed a more favorable healing pattern of the injured nerve to healing.

The study by Yuca et al. (2020) used laser with the energy of 4 J/cm² for 32 seconds in 21 consecutive days, this device has a wavelength of 850nm. In the ozone group, through intraperitoneal insufflation, the gas mixture of oxygen and oxon, 97.5% and 2.5%, respectively, was insufflated at a dose of 2mL (80μm/mL) for 21 days, once every 2 days. In this perspective, this study obtained better results in the ozone therapy group compared to the control and laser group, also, it was shown that ozone should not be performed with a mixture of ozone gas and saline.

This review included favorable results for both therapeutic modalities. Laser photobiomodulation and ozone therapy have demonstrated efficacy in the tissue repair process, with a slight superiority of ozone gas. However, due to the diversity of types of tissues evaluated in the experimental models, it was not possible to carry out a statistical analysis of the reported results with metanalysis, despite the protocol similarity pattern in all studies.

Ozone is known to reduce the oxidative stress of inflammation and increase partial tissue oxygen (Bocci, 2006; Yildirim et al., 2014). This process starts when ozone passes into the bloodstream. At this time, some changes can be observed in cells and tissues. At low doses, ozone is able to fight oxygen free radicals and increase the enzymatic synthesis of antioxidant proteins, promoting control of oxidative stress (Güner et al., 2016). Furthermore, in response to oxidative stress, ozone gas increases the level of 2-3-diphosphoglycerate, which reduces the degree of affinity of hemoglobin with oxygen molecules, increasing circulating O_2 levels, promoting abundant oxygen access to previously hypoxic cells, contributing to the action of the immune system in the infected area (Rowen, 2018). Three studies (Kazancioglu et al., 2013; Yucesoy et al., 2017; Yuca et al., 2020) demonstrated significative results for ozone. In this sense, the antibacterial and stimulating properties of the immune system were evidenced, especially in the prevention of infection allowing the organism to develop the stages of tissue repair physiologically.

In the studies analyzed, the most used method for the treatment of wounds was the insufflation of ozone gas, being perilesional (Alan et al., 2015; Kazancioglu et al., 2013; Bayer et al., 2017), buccal (Yucesoy et al., 2017), and intraperitoneal (Yuca et al., 2020). However, the Chagas' study in 2015 demonstrated favorable results in wound healing with topical application of ozonated oil compared to the control group and documented a significant difference for hyperemia, inflammatory infiltrate, collagen, erosion, and inflammation of the epidermis and dermis. Also, the authors reported the animals' self-mutilation due to the unpleasant odor caused by ozonized oil during the 15 days of their study (Chagas & Mira, 2015).

The absorption of energy from laser photobiomodulation on tissues is able to stimulate the action of mitochondria in order to induce greater production of ATP in addition to regulating DNA and RNA synthesis with consequent cell proliferation (Alan et al., 2015). An *in vitro* study demonstrated that there is greater stimulation of synthesis collagen, the release of growth factors, and the transformation of fibroblasts into myofibroblasts (Hopkins et al., 2014). The findings of the studies in this systematic review corroborated some of these effects in the evaluated tissues submitted to laser photobiomodulation and ozone therapy.

Bayer et al. (2017) highlighted that there is still a lack of consensus on the dosages of therapies. Some conflicting results from different protocols demonstrate the importance of advancing research on this topic. Furthermore, none of the articles selected in this review used the high-frequency generator associated with the laser, unlike the study by Sá et al. (2010), the authors demonstrated an improvement in the healing pattern after this therapeutic association in cutaneous wounds of rats in the period of 7 days. However, according to Sousa et al. (2015), it is clear that the use of only the high-frequency generator as a modulatory therapy, with the purpose of accelerating tissue repair, showed inferior results compared to the low-frequency laser of 660nm, either 8J/cm^2 or 5J/cm^2, after 14 days of study.

Concerning the application of Guideline ARRIVE, three studies presented similar results, with high methodological quality, which makes them reproducible, transparent articles, ordered logically, well conducted and with precise objectives. Two studies presented similar results with limitations in methodology (sample size and allocating animals to experimental groups) and results (numbers analysed and adverse events). This is probably because both studies belong to the same research group. However, it is worth mentioning that despite these limitations, the studies have the ability to be reproduced.

The number of studies on laser and/or ozone is very large and the two therapeutic modalities have been used in the health area for many years. The inclusion and non-inclusion criteria of this review, in order to filter methodologies that can serve as a basis for other projects, demonstrated the existence of a small number of studies already carried out with rats that compared these modulatory therapies.

Some limitations were observed in this study, such as the variety of protocols, types of tissues and population (rats) in the selected studies. Despite these limitations, it is strongly recommended to conduct new controlled clinical trials aimed at the comparative use among laser photobiomodulation and ozone gas.

5. Final Considerations

Experimental studies included in this systematic review that used laser photobiomodulation and ozone gas comparatively, revealed favorable effects of these modulatory therapies on tissue repair. However, the variables analyzed in each study were diverse and it was difficult to carry out statistical treatment of the data. The laser and ozone promoted better results than those observed in the groups that were not treated with these therapies and, proportionally, the ozone gas stood out more. In addition, there were few studies comparing the effectiveness of laser photobiomodulation and ozone therapy on tissue healing.

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