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LOW-LEVEL RED-LIGHT THERAPY FOR CONTROL, ONSET AND PROGRESSION OF MYOPIA: AN UPDATED REVIEW

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Abstract: Objective: To investigate the efficacy, mechanisms of action and potential benefits of repetitive low-level red-light therapy (RLRL) in controlling the onset and progression of myopia. **Methods**: Bibliographic review through the PubMed database, the PVO research strategy (Population or research problem, Variables and Outcome) was adopted, with the guiding question: "How does low-level repetitive red-light therapy affect the onset and the progression of myopia in different populations?". The initial search resulted in 32 articles, of which 15 were selected after applying inclusion and exclusion criteria. **Review**: It is demonstrated that RLRL presents promising results in controlling myopia, delaying its progression without generating significant adverse effects. Red light stimulates the release of dopamine by the retina, regulating the axial growth of the eye and influencing the pathophysiological processes of myopia. **Final Considerations**: The importance of additional research into the effectiveness of RLRL in different age groups and severities of myopia, as well as its long-term effects, is highlighted. Despite the promising results, more studies are needed to optimize its clinical application and ensure consistent and safe results for patients.
Keywords: Repetitive low-level red-light therapy, photobiomodulation, myopia.

INTRODUCTION

Myopia is the most prevalent form of refractive error, having a major negative impact on visual function, generating blurred vision (Youssef et al., 2024). Studies estimate that the number of myopic people in the world will be 50% by 2050 and 10% of the world's population will have high myopia (Wang et al., 2023). This refractive error is related to an important risk of disorders that permanently impair vision, such as myopathic maculopathy, glaucoma, staphyloma and retinal detachment (Xiong et al., 2021).

In recent years, increased time spent outdoors in bright light has been found to be an effective protective factor against myopia. Several therapies have been proposed for myopia control; however, the feasibility of current strategies continues to be limited by adverse effects and inconveniences. In this scenario, low-level red-light therapy (RLRL) emerged, which has recently emerged as a new treatment method for myopia control (Xiong et al., 2022). Given this, some studies point to low-level repetitive red-light therapy as an effective treatment with no documented functional or structural damage (Dong et al., 2022). This therapy promotes the correction of imbalances in the growth of the eyeball, reducing the elongation of the eye axis and controlling the degree of myopia (Deng et al., 2024).

Studies with repetitive low-level red-light therapy are based on verifying the effectiveness of this new therapeutic method for controlling myopia, its safety and adverse effects. The method in question showed positive results in delaying the progression of myopia, discovering that red light, at a frequency of 650 nm, is capable of stimulating the retina to release more dopamine, which performs the function of inhibiting the longitudinal growth of the globe. eyepiece, which consequently produced a decrease in the degree of refractive error. In addition to the demonstrated efficacy, the studies also revealed advantages regarding the safety of using red light, as it did not generate significant adverse effects in the exposed groups and it is a non-invasive method (Deng et al., 2024).

Despite the innovation and possibilities with this therapeutic method, the literature on the subject may still be limited, especially when observing limitations in long-term evaluation. Many studies do not present patient follow-up times for sufficiently adequate periods to assess the stability of the results and possible adverse effects and in some cases serious adverse effects (Augustyn; Teper; Wylegala, 2023).

Treatment protocols that are still poorly established and the lack of concrete guidelines on how to carry out therapy can make it difficult to apply in clinical practice, in addition to not adequately addressing how therapy results can vary according to age group, severity of myopia and individual factors. Therefore, the purpose of this study is to investigate how repetitive low-level red-light therapy affects the onset and progression of myopia in different populations.

METHODOLOGY

Literature review developed following the criteria of the PVO strategy, short for Population or research problem, Variables and Result. This strategy was adopted to guide the investigation, guided by the following research question: "How does repetitive low-level red-light therapy affect the onset and progression of myopia in different populations?" According to the parameters mentioned, the population or research problem involves patients with myopia who require Low Level Repetitive Red-Light Therapy to control the progression of the disease. The searches were carried out in the PubMed Central (PMC) database. The search terms were used, combined with the Boolean term "AND" and "OR" through the following search strategy: (("Repeated Low-Level Red-Light Therapy") OR (Photobiomodulation) AND (Myopia). From this research strategy, 32 articles were identified by applying the filter from the last 5 years. These articles were then evaluated according to pre-established selection criteria. The inclusion criteria adopted were: articles in English, published between 2019 and 2024, that addressed the themes proposed for this research, including review studies, meta-analysis, observational studies and clinical trials available in full. The exclusion criteria were: duplicate articles, articles available only in abstract form that did not directly address the topic. proposed study and that did not meet the remaining inclusion criteria. In total, 15 articles were selected for the present study.

REVISION

Low-level red-light therapy (RLRL) has generated interest as a potential approach for the control and progression of myopia. Red light, characterized by its monochromaticity, offers a unique molecular specificity that can be harnessed to modulate ocular biological processes (Zhu et al., 2023).

Repetitive low-level red-light therapy is a modern, non-invasive intervention that has shown efficacy and safety in slowing the progression of myopia in children (Zhou et al., 2023). Empirical studies indicate that oxidative stress and inflammation are key factors in altering the regulatory pathways of this refractive pathology, impacting neuromodulators, such as nitric oxide and dopamine, which can also be modulated by photobiomodulation through exposure to natural light or pulse of low-level red light (Deng et al., 2023; Xiong et al., 2021; Youssef et al., 2024).

Myopia is the most common refractive error, causing blurred vision and negatively impacting visual function. The threshold for myopia progression is a spherical equivalent refraction (SER) of -1.00 diopters (D) or less. The main feature of irreversible vision loss associated with high myopia is choroidal thinning. Studies in animals and humans indicate that the choroid plays a crucial role in controlling the development of the ocular refractive system. Therefore, there is an urgent need for more effective and practical treatments to halt the progression of myopia. Although increased exposure to outdoor light can be successfully implemented through national outdoor programs, its implementation remains inadequate in certain circumstances. On the other hand, optimizing architectural lighting or developing light therapy devices requires a comprehensive understanding of the benefits and side effects of light characteristics on ocular growth and neurophysiology (Xiong et al., 2023).

The RLRL entails the use of lasers or light-emitting diodes (LEDs) to deliver light with a specific wavelength, approximately 650 nanometers (Augustyn, Teper, and Wylegala, 2023). At this wavelength, red light has the ability to stimulate the retina's synthesis and release of dopamine, a neurotransmitter that plays a crucial role in regulating eye growth, refractive development, and visual signal transduction (Zhu et al., 2023; Deng et al., 2024; Activation of dopamine receptors, such as D1, D2, D4, and D5 sub receptors, is closely linked to myopia progression, with evidence indicating that activation of D2 receptors can promote myopia, while activation of D1 receptors can induce hyperopia. Furthermore, there is a linear relationship between red light intensity and dopamine release (Zhu et al., 2023).

According to Zhu et al. (2023), the response to red light presents a U-shaped curve, where low doses can promote positive responses, while high doses can inhibit biological processes. This hormetic curve has been shown to be more effective in predicting biological responses within therapeutic limits, compared to traditional linear curves. Dopamine release may promote choroidal thickening and retard ocular growth, potentially through the release of nitric oxide by the retina and choroid (Liu et al., 2024; Xuan et al., 2022). Other mechanisms involve the regulation of circadian rhythms, in which light plays a crucial role in modulating eye growth, with dopamine acting as a critical mediator of these rhythms.

Through photobiomodulation, red light can affect ocular tissues, potentially triggering a series of beneficial effects, such as regulating the axial growth of the eye and modulating the inflammatory response (Zhu et al., 2023). A meta-analysis encompassing six studies and a total of 820 patients, with the aim of evaluating the efficacy and safety of low-level red-light therapy in controlling myopia progression. Their results revealed a significant reduction in ocular axis widening in the group undergoing red light therapy compared to the control group, as well as a decrease in spherical equivalent refractive error. Furthermore, the study highlighted the advantages of red-light therapy in terms of safety and tolerability, with few reports of adverse reactions (Deng et al., 2024).

Such findings suggest that low-level red-light therapy may offer an innovative and effective approach to treating myopia by directly influencing the biological mechanisms underlying its progression (Zhu et al., 2023). According to Xiong et al. (2021, 2022) and Youssef et al. (2024), red light therapy has been shown to be more effective than other methods. Xiong et al. (2021) report that the exposed group showed a significant difference in cycloplegic spherical equivalence, being smaller than in the control group, and also obtained a slightly smaller axial length compared to the control and orthokeratology groups.

Studies by Xiong et al. (2022), which lasted 24 months, demonstrated better control in axial elongation and progression of cycloplegic spherical equivalence compared to single vision glasses. After stopping therapy, the exposed group showed a rebound effect, associated with sudden discontinuation of treatment, which can be minimized with gradual withdrawal. To analyze the magnitude of this effect, it is essential to consider the natural deceleration of ocular axial growth with age. Youssef et al. (2024) found that orthokeratology is related to keratitis, atropine ocular solutions with photophobia, and other methods with scotomas as adverse effects; in contrast, red light therapy has had no documented significant adverse effects.

Low-level red-light therapy also involves crucial safety and practical considerations in myopia management (Wang et al., 2023). The devices used, such as Eyerising, employ semiconductor laser diodes to emit low-level red light with a specific wavelength, considered safe for direct ocular exposure, according to international regulations. Light power is carefully controlled to ensure there is no thermal risk to the retina, ensuring the treatment is safe for both adults and children (Liu et al., 2022).

In addition to safety, adherence to treatment is essential to achieve effective results. Research carried out by Xiong et al. (2022) demonstrate that high adherence to treatment is associated with better results, such as reducing myopia progression and even reversing axial shortening in children. The use of the device is recommended in two daily sessions of 3 minutes each, with a 4-hour break, for 5 days a week (Wang et al., 2023; Zhou et al., 2023).

The ease of use of the device, characterized by short treatment sessions and flexible breaks between them, and the support of an automated diary to record sessions, contribute significantly to more consistent adherence (Xiong et al., 2022).

Another important advantage is the absence of significant adverse side effects. Clinical studies, conducted in both adults and children, have reported no complications related to the use of RLRL therapy, offering additional assurance of its safety and effectiveness in controlling myopia (Zhou et al., 2023). These findings reinforce the practical feasibility and safety of using low-level red light as a promising therapeutic approach for the management of myopia (Wang et al., 2023).

The need for research and the development of efficient therapies arises from the unfavorable prognosis in the natural evolution of this refractive problem, with the potential to lead the individual to more serious conditions, such as elongation of the eyeball, retinal detachment, macular openings, vitreous hemorrhage, edema type grape, macular degenerations and, in extreme cases, blindness (Deng et al., 2023). It is expected that, in the coming years, it will be possible to more accurately determine the indications for optimal use, the long-term beneficial and adverse effects, and the potential rebound effect of this therapy (Youssef et al., 2024). Investigations of outcomes with corneal remodeling lenses, low-concentration atropine eye drops, glasses, and defocusing soft contact lenses are also needed (Deng et al., 2023).

FINAL CONSIDERATIONS

The RLRL has been shown to be effective in slowing the progression of myopia, offering a promising alternative to conventional therapies. Studies have highlighted the ability of red light to stimulate the release of dopamine by the retina, thus regulating the axial growth of the eye and directly influencing the pathophysiological processes involved in myopia. Furthermore, RLRL has been shown to be safe and well tolerated, with few reports of significant adverse effects. Research and development of effective therapies are crucial due to the adverse prognosis associated with this refractive problem, which can evolve into serious conditions such as elongation of the eyeball, retinal detachment, among other complications, which can lead to blindness. The relevance of additional research on the topic lies in the urgency of finding more effective and practical treatments to halt the progression of myopia, especially given the current increase in the prevalence of this refractive visual disorder.

Better understanding the mechanisms of action of RLRL and its short- and long-term impact is essential to optimize its clinical application and ensure consistent and safe results for patients. Future investigations are expected to clarify the best indications for therapy, its long-term benefits and risks, and possible rebound effects. Evaluations of techniques such as corneal reshaping lenses and low-concentration atropine eye drops are also needed.

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