Use of Photobiomodulation to Treat Eyesight

Date: 17/05/2024

Introduction

Photobiomodulation (PBM) therapy, also known as low-level light therapy, is increasingly gaining attention as a non-invasive treatment for various ocular conditions. This therapy employs low-intensity light at specific wavelengths, primarily in the visible to near-infrared (NIR) spectrum, to influence cellular processes. The primary target of this light absorption is cytochrome c oxidase, a crucial enzyme in the mitochondrial electron transport chain. Activation of cytochrome c oxidase triggers a series of biochemical reactions that lead to enhanced cellular metabolism, increased production of adenosine triphosphate (ATP), reduced levels of reactive oxygen species (ROS), and boosted antioxidant protection (NCBI). These effects collectively contribute to the restoration and maintenance of cellular function.

PBM has demonstrated significant potential in treating retinal diseases such as age-related macular degeneration (AMD) and diabetic retinopathy (DR). For instance, studies have shown that PBM can protect the retina from photoreceptor degeneration and improve visual acuity in patients with dry AMD (Retina Today). Additionally, the LIGHTSITE clinical trials have provided compelling evidence of PBM's efficacy in enhancing visual function and reducing disease progression in AMD patients (PubMed).

Beyond its efficacy, PBM is noted for its favourable safety profile. Extensive research in both animal and human studies has shown minimal adverse effects, making it a promising candidate for widespread clinical application (NCBI). The non-invasive nature of PBM, combined with its ability to penetrate specific tissues and aid in cellular recovery, positions it as a valuable tool in the treatment of various ocular conditions.

This report aims to provide a comprehensive overview of the mechanisms, clinical applications, and efficacy of PBM in treating eyesight, supported by data from recent studies and clinical trials.

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Mechanisms of Photobiomodulation

Cellular and Molecular Mechanisms

Photobiomodulation (PBM) therapy employs low-intensity light at specific wavelengths, primarily in the visible to near-infrared (NIR) range, to influence cellular processes. The primary target for light absorption in the red-to-NIR region is cytochrome c oxidase (CcO), a key component of the mitochondrial electron transport pathway (NCBI). Activation of CcO initiates a series of biochemical reactions that result in increased production of adenosine triphosphate (ATP), decreased levels of reactive oxygen species (ROS), and enhanced antioxidant protection. These factors contribute to the restoration of cellular function.

PBM affects numerous cellular functions, such as gene expression, cellular growth, proliferation, survival, and differentiation (NCBI). The metabolic processes of the eyes and neurons heavily depend on cytochrome c oxidase for energy production. PBM with LED technology has the ability to penetrate these specific tissues and aid in the recuperation of neurons affected by methanol intoxication, optic nerve trauma, neuropathy, retinal injuries, pigmentosa, and macular degeneration (NCBI).

Impact on Retinal Cells

Photobiomodulation has been shown to protect the retina from light-induced photoreceptor degeneration. Studies have demonstrated that PBM can reduce drusen volume and improve visual acuity and contrast sensitivity in dry age-related macular degeneration (AMD) (Retina Today). For instance, a study by Merry et al. (2017) found that PBM reduced drusen volume by 32% and improved visual acuity by 8 letters on the ETDRS chart in patients with dry AMD (Acta Ophthalmol).

In another study, Eells et al. (2004) demonstrated that mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy was effective, showing a 25% improvement in wound closure rates (Mitochondrion). This suggests that PBM can enhance the healing process in retinal cells by improving mitochondrial function and reducing oxidative stress.

Clinical Outcomes and Efficacy

The LIGHTSITE III study evaluated multiwavelength photobiomodulation (PBM) therapy in nonexudative (dry) age-related macular degeneration (AMD) using the LumiThera Valeda Light Delivery System. The study was a randomized, controlled trial to assess the safety and effectiveness of PBM in dry AMD. Subjects were given multiwavelength PBM (590, 660, and 850 nm) or Sham treatment delivered in a series of nine sessions over 3 to 5 weeks every four months over 24 months (PubMed).

The results showed that the PBM group had a significant improvement in best-corrected visual acuity (BCVA) by an average of 5.5 letters compared to the Sham group. Additionally, the PBM group showed a significant decrease in new onset geographic atrophy by 15% ($P = 0.024$, Fisher exact test, odds ratio 9.4). A favourable safety profile was observed, with minimal safety risks and high patient compliance (PubMed).

Safety and Side Effects

Thorough examination of animals and humans has not revealed any adverse effects of PBM using LEDs. This suggests that PBM is a safe and efficacious method for various applications in the fields of ophthalmology and neurology (NCBI). The LIGHTSITE III study also reported minimal safety risks and high patient compliance, with 80% of the patients completing the trial (PubMed).

Future Directions and Research

Significant progress has been made in understanding the mechanisms underlying the success of photobiomodulation (PBM). However, new signal transduction pathways are continually being explored, and there is still much to uncover in this complex puzzle (NCBI). Emerging approaches to AMD treatments, such as the use of the Valeda system, have

demonstrated sustained improvement in vision and a reduction in rates of new geographic atrophy in patients with intermediate dry AMD across two years (Macular).

To sum up, photobiomodulation (PBM) therapy presents a promising and potent approach to modulate biological functions via low-power light wavelengths within the red to near-infrared spectrum. The ability of PBM to enhance mitochondrial function, reduce oxidative stress, and improve cellular function makes it a valuable tool in the treatment of various retinal conditions. Further research is needed to fully understand the mechanisms of PBM and to explore its potential in other areas of ophthalmology and neurology.

Clinical Applications in Ophthalmology: Use of Photobiomodulation to Treat Eyesight

Age-Related Macular Degeneration (AMD)

Dry AMD

Photobiomodulation (PBM) has shown promising results in treating dry age-related macular degeneration (AMD). The LIGHTSITE III clinical trial, a prospective, double-masked, randomised, multicentre study, evaluated the efficacy of PBM in improving vision in dry AMD patients. Conducted at 10 US retinal centres, the trial involved 100 subjects with a mean age of 75 years and a mean dry AMD duration of 4.9 years before enrolment. The primary efficacy endpoint, best corrected visual acuity (BCVA), was evaluated at 13 months. The results demonstrated a statistically significant improvement in BCVA in the PBM treatment group compared to the sham-treatment group ($P<0.003$). Additionally, a sustained mean increase in ETDRS letter score of 5.5 letters from baseline was observed at the 13-month timepoint in the PBM-treated subjects ($P<0.0001$) (Eyewire News).

The LIGHTSITE II European trial also demonstrated similar sustained improvements in visual benefits with PBM treatments, with a mean 5.5 letter improvement in BCVA, indicating the potential of PBM to offer non-invasive treatment options for dry AMD patients (Eyewire News).

Mechanism of Action

The proposed mechanisms of action for PBM in treating AMD include enhanced photoreceptor mitochondrial function, counteracting inflammation, and enhanced supporting cell function (Dovepress). Studies have shown that PBM can significantly increase BCVA and contrast sensitivity (CS) in patients with dry AMD and reduce drusen volume, indicating that low-energy red light exposure may alleviate the progression of dry AMD and improve visual function (NCBI).

Diabetic Retinopathy (DR)

Diabetic Macular Oedema (DME)

PBM has also been explored as a treatment for diabetic macular oedema (DME). A pilot study presented at the 2017 ARVO Annual Meeting demonstrated that 670 nm photobiomodulation could be a potential therapy for diabetic macular oedema (Dovepress). Another study showed that exposure to red laser light (670 nm; 18 J/cm2, 5 weeks) significantly improved DME and reduced foveal thickness (NCBI).

Mechanism of Action

The mechanisms by which PBM exerts its effects in diabetic retinopathy include inhibition of long-term structural and functional lesions, as demonstrated in a study where PBM inhibited lesions of diabetic retinopathy (Dovepress). Enhanced mitochondrial function and anti-inflammatory effects are also proposed mechanisms (Dovepress).

Clinical Trials and Studies

LIGHTSITE III

The LIGHTSITE III trial, conducted at 10 US retinal centres, aimed to treat dry AMD subjects with PBM every 4 months for 24 months. The primary efficacy endpoint, BCVA, was evaluated at 13 months, showing statistically significant improvement in the PBM treatment group over the sham-treatment group ($P<0.003$). A sustained mean increase in ETDRS letter score of 5.5 letters from baseline was observed at the 13-month timepoint in the PBM-treated subjects ($P<0.0001$) (Eyewire News).

LIGHTSITE II

The LIGHTSITE II European trial demonstrated similar sustained improvements in visual benefits with PBM treatments, with a mean 5.5 letter improvement in BCVA, indicating the potential of PBM to offer non-invasive treatment options for dry AMD patients (Eyewire News).

Other Studies

A study by Eells et al. explored the use of 670 nm photobiomodulation as a therapy for diabetic macular oedema, presented at the 2017 ARVO Annual Meeting (Dovepress). Another study by Tang et al. demonstrated the efficacy of PBM in treating non-centre-involving diabetic macular oedema (Dovepress).

Summary of Available Articles

Age-Related Macular Degeneration

- A summary of available articles describing the application of PBM for age-related macular degeneration includes details on subjects, eyes treated, wavelength, device used, dose and delivery parameters, and results of the studies (Dovepress).

Diabetic Retinopathy

- Similarly, a summary of available articles describing the application of PBM for diabetic retinopathy includes details on subjects, eyes treated, wavelength, device used, dose and delivery parameters, and results of the studies (Dovepress).

Future Directions

Emerging Therapies

- Emerging therapies in non-exudative age-related macular degeneration include PBM as a potential treatment option. A review by Samanta et al. highlighted the potential of PBM in treating non-exudative AMD (Dovepress).

Clinical Implications

- The clinical implications of PBM in treating retinal diseases are significant, with studies demonstrating improvements in visual function and reduction in disease

progression. The non-invasive nature of PBM makes it an attractive option for patients with limited treatment options (Eyewire News).

To sum up, PBM has shown promising results in treating retinal diseases such as age-related macular degeneration and diabetic retinopathy. Clinical trials and studies have demonstrated significant improvements in visual function and reduction in disease progression, highlighting the potential of PBM as a non-invasive treatment option for patients with limited treatment options.

Evidence and Efficacy of Photobiomodulation in Treating Eyesight

Mechanism of Action

Photobiomodulation (PBM), also known as low-level light therapy, utilizes visible and near-infrared light (590 nm to 1,000 nm) to stimulate cellular activity. The primary mechanism involves the absorption of photons by cytochrome c oxidase, an enzyme in the mitochondria (the energy-producing parts of cells). This process is believed to enhance cellular metabolism and reduce inflammation (Retinal Physician). This mechanism is particularly relevant in the context of age-related macular degeneration (AMD), where improved mitochondrial function in retinal cells could potentially slow disease progression.

Clinical Trials and Visual Acuity Improvements

TORPA Trials

The TORPA 1 and TORPA 2 trials were among the first to investigate the effects of PBM on visual acuity (VA) in AMD patients. The TORPA 1 trial demonstrated VA improvements in a small cohort, while the TORPA 2 trial, which included a larger cohort, also reported VA improvements from baseline. However, both studies were limited by the lack of randomization and comparator groups (Retinal Physician).

LIGHTSITE Trials

The LIGHTSITE I trial introduced a more rigorous study design, utilizing the Valeda Light Delivery System and a randomized sham-controlled approach. This trial found initial increases in VA, but these gains declined to near baseline values at six months, indicating the need for repeat treatments. Additionally, a reduction in drusen volume was observed in the PBM-treated group compared to controls (Retinal Physician).

The LIGHTSITE II trial, a sham-controlled, prospective, multicentre study, further validated these findings. PBM-treated eyes showed increases in VA, stable drusen volume, and reductions in geographic atrophy (GA) lesion growth compared to sham-treated eyes (Retinal Physician).

Long-term Efficacy: LIGHTSITE III Trial

The LIGHTSITE III trial provided the most comprehensive data to date, enrolling 100 subjects with intermediate AMD and treating them with PBM over a 24-month period. At 13 months, PBM-treated eyes showed a significant improvement in VA of 5.4 letters from baseline. This improvement was sustained at 24 months, with an average gain of 5.9 letters. Additionally, the trial reported a reduction in the number of subjects losing more than 5

letters (7% in the PBM group vs. 18% in the sham group) and a lower progression rate to GA (6.8% in the PBM group vs. 24% in the sham group) (Retinal Physician).

Safety and Noninvasive Nature

PBM is well-established in other therapeutic areas, and its application in ophthalmology is evolving. The noninvasive nature of PBM, particularly with the Valeda system, offers a significant advantage, allowing for earlier intervention in the disease cycle. This early treatment is crucial for slowing or halting disease progression before significant tissue loss occurs (Retinal Physician).

Future Directions and Ongoing Research

The retina community is eagerly anticipating further data from higher-powered PBM studies to assess its clinical efficacy across different settings and stages of AMD. The potential for at-home treatment with a noninvasive mechanism is particularly appealing, addressing an unmet need in the management of AMD (Retinal Physician).

Recent advances in photobiology and bioenergetics, such as the discovery of photoneuromodulation by cytochrome c oxidase, have propelled the adoption of near-infrared (NIR) light therapy. NIR light has been shown to increase cytochrome oxidase and superoxide dismutase activities, suggesting its role in inducing metabolic and antioxidant benefits. Additionally, NIR light may enhance cerebral blood flow and cognitive functions without adverse effects, further supporting its use in treating visual and neurological conditions (PubMed).

Summary of Findings

- **Mechanism**: PBM enhances cellular metabolism and reduces inflammation through cytochrome c oxidase activation.
- **TORPA Trials**: Demonstrated VA improvements but lacked randomization and comparator groups.
- **LIGHTSITE Trials**: Showed sustained VA improvements, reduced drusen volume, and slower GA progression.
- **Safety**: Noninvasive and suitable for early intervention in AMD.
- **Future Research**: Higher-powered studies and at-home treatment options are being explored.

The LIGHTSITE III trial's results are particularly promising, offering one of the first modalities that may reduce AMD progression and visual decline in the early stages of the disease (Retinal Physician).

To Sum Up

To sum up, photobiomodulation (PBM) therapy offers a promising and potent approach to treating retinal diseases such as age-related macular degeneration (AMD) and diabetic retinopathy (DR). By enhancing mitochondrial function and reducing oxidative stress, PBM contributes to improved cellular function and visual outcomes. Clinical trials, such as the LIGHTSITE III study, have demonstrated significant improvements in visual acuity and a

reduction in disease progression among patients undergoing PBM treatment (Retinal Physician).

Moreover, the safety and non-invasive nature of PBM make it an attractive option for patients with limited treatment alternatives. The potential for at-home treatments further enhances its appeal, addressing an unmet need in the management of ocular diseases (Eyewire News).

As research continues to uncover the intricate mechanisms of PBM and its broader applications, it is expected that this therapy will play a crucial role in the future of ophthalmologic treatments. Continued exploration and higher-powered studies will be essential in validating and expanding the clinical use of PBM, potentially transforming the landscape of retinal disease management (PubMed).

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