

Light therapy in retinal vascular disease

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Abstract

Objectives: To describe and appraise the latest reports on light devices currently used for the treatment of diabetic retinopathy and age-related macular degeneration.

Methods: The present review was conducted using four national and international databases - PubMed, Scielo, Medline and Cochrane. Initial set of clinical or experimental trials was screened based on title and abstracts, followed by full text analysis and critical review.

Results: Five main articles were included. Each report's methods and results are described in table 1. Light-mask appears to be effective in the treatment of diabetic retinopathy and diabetic macular edema. A recent trial is being conducted to evaluate its efficacy in early age-related macular degeneration, although no results are available yet.

Conclusion: Based on recent latest clinical trials, light-mask shows promising results in the treatment of diabetic retinopathy and diabetic macular edema.

Introduction

The outer retina is an avascular layer that is predominantly composed by photoreceptors. Its vascular supply depends on simple diffusion, relying in the integrity of choroidal circulation [1].

Rods are highly metabolic active [2,3] consuming the most oxygen delivered to the retina. In bright light, oxygen consumption decreases due to a drop in the energy required by these cells [4]. In contrast, cones seem to consume the same amount of O₂ as it would in dark environments, and energy requirement is minimally affect by differences in luminosity.

Light is a novel, simple approach that may be used to alter retinal hypoxia [5,6], which is a major component in retinal vascular diseases such as diabetes and age-related macular degeneration (AMD). Evidences show that inner segment hypoxia is sufficient to trigger microvascular changes [7], which may be further enhanced by choroidal vasculopathy, an early feature of systemic vascular diseases, such as diabetes [8].

In this review, the authors will present the latest evidence on how light can affect vascular integrity and disease progression based on recent experimental and clinical trials.

Methods

A retrospective, descriptive review of current models using light devices to prevent nocturnal retinal hypoxia was conducted, based on recent clinical trials available in literature. Four national and international databases were consulted (PubMed, Scielo, Medline, and Cochrane). An initial screen yielded a total of twenty three articles, each meeting at least one of the following criteria:

- (1) retinal changes in diabetes mellitus and age-related macular degeneration,
- (2) light-masks for the treatment of retinal hypoxia, and
- (3) rod metabolism.

After secondary analysis, only 5 clinical trials were considered to meet two or three of the above criteria. These were included in this review.

Results and discussion

The idea to prevent retinal hypoxia using light therapy during sleep has been promising, although there is little evidence to support it. In 2008, Okawa, et al. [4] showed that mice retinal oxygen consumption is decreased approximately by half in the presence of bright light. On the contrary, using diabetic mice in a 12-week period, Kur, et al. [9] showed that a 12:12 hour light-adapted photocycle (30 lux during day, and 3 lux during night) did not prevent the progression of neuronal and glial abnormalities when compared to control group (30 lux during day, and 0 lux during night). However, the authors postulate that a 12 week period may have been insufficient to detect positive effects with this intervention, although some studies described below report positive results during the same period of intervention.

Sahni, et al. [10] evaluated the use of a light-mask (504 nm wavelength, 80 cd/m², for 8 hours nightly) in two different age-groups with healthy participants compared to a third group, composed by patients with diabetic macular edema. Several parameters were evaluated after a three month period, including psychological assessment. Intolerance to light and sleep disturbance were reported, which caused a withdrawal of 6 patients. However, in those with macular edema, there was a reduction of optical coherence tomography mean central

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Key words: light-mask, diabetic macular edema, rods, retinal hypoxia, dark adaptation

Received: December 05, 2017; **Accepted:** December 26, 2017; **Published:** December 30, 2017

Table 1. Depicts the latest and current trials concerning the use of a light device during sleep and the effect on progression of diabetic retinopathy, diabetic macular edema and early AMD.

Studies	Retinal disease	Light device	Results
Arden, <i>et al.</i> (2010) [16]	Diabetic maculopathy	Trans-lid retinal illumination	12 patients enrolled in a 3 month-period. Reduction in tritan thresholds and the incidence of hemorrhage and microaneurysms (p=0.03).
Arden, <i>et al.</i> (2011) [17]	Diabetic maculopathy	Sleep mask (505 nm)	34 patients enrolled in a 6 month-period. Regression of macular edema (p=0.01) and improvement of visual acuity, achromatic contrast sensitivity, and microperimetric thresholds.
Sivaprasad, <i>et al.</i> (2014) [18]	Non-central diabetic maculopathy	Sleep mask (PolyPhotonix Medical Ltd)	Results are still not available.
McKeague, <i>et al.</i> (2014) [14]	Early AMD	Sleep mask (PolyPhotonix Medical Ltd)	Results are still not available.
Sahni, <i>et al.</i> (2017) [11]	Diabetic maculopathy	Sleep mask (PolyPhotonix Medical Ltd)	46 patients enrolled in 4 month-period (1 month for recovery). Beneficial effect on OCT CST (p=0.001) and OCT maxCT (p=0.05). Psychological wellbeing worsened in all groups (p<0.05).

subfield thickness (OCT CST; p=0.001) and mean thickness of OCT subfield with maximal pathology (OCT maxST; p=0.05) at months 3 and 4, as well as cyst resolution/reduction in 67% of patients.

Even though sleep and psychological wellbeing were compromised, the authors reported no major safety precaution. Further, the rise in PO₂ with this approach does not seem to harm the rods, even in prolonged periods of illumination [11].

Noctura 400[®] (PolyPhotonix Medical Ltd, Sedgefield, UK) is a light-mask recently developed for the treatment of diabetic retinopathy and diabetic macular edema, and is currently being (or have been) used in large clinical trials, with promising results. It consists in a light-emitting diode placed inside a fabric mask, originally intended for a 12 week period during night-time sleep [12]. Although there is a focus on diabetes, a recent protocol [13] has been developed for patients with early AMD, and is currently in progress. Vascular compromise in patients with AMD may correlate to the thickness of Bruch's membrane, which further impair oxygen diffusion to the outer segment [14]. A newer version, Noctura 500, has been designed for wet AMD. Currently, however, no evidence is available for its use in this disease.

The adoption of a light-mask may also have an impact on health care cost. Patients with proliferative diabetic retinopathy typically require costly treatments, such as laser photocoagulation or repeated sessions of intra-ocular anti-vascular endothelial growth factor (anti-VEGF). Light therapy may potentially replace these options in the future (Table 1) [10,13,15-17].

Conclusion

Latest clinical trials seem to favor effect of low-level night-time light therapy in patients with diabetic maculopathy, non-central diabetic maculopathy and early AMD. To our knowledge, this was the first review on this subject, concerning the newest experimental protocols of light therapy. The approach of this review is to organize the information needed for future research.

Acknowledgement

The authors declare no conflict of interest.

No financial support was required for the development of this article.

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