Original Article

A Pilot Study: Assessment of Therapeutic Effects 670 nm Photobiomodulation on Amblyopia

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ABSTRACT

Purpose: To evaluate positive effects of photobiomodulation in amblyopia treatment in patients with 8-13 year of age.

Study Design: interventional case series.

Place and Duration of Study: Shahid Beheshti University of Medical Sciences, Iran.

Methods: This study was conducted on 16 subjects with strabismic amblyopia. Subjects were assigned to two groups: Photobiomodulation (PBM) and control group. In the PBM group, patients used a portable device (Warp 10, Quantum device) in home 3 times a week. The amblyopic eye were irradiated by a device which emitted 670 nm red light with 25 Joules/cm2 energy for 4 minutes. After irradiation, patients performed near work for 10 minutes. In the control group, patients were treated by using part time occlusion of non-amblyopic eye and near work for 3 months. Ophthalmic assessments including best corrected visual acuity (BCVA), refractive evaluation, slit lamp biomicroscopy, and fundoscopy were performed before and four weeks, and three months after treatment.

Results: In the PBM group, the mean baseline BCVA was 0.24 ± 0.15 that improved to 0.49 ±0.24 in the third month after treatment. In the control group, the mean initial BCVA was 0.30 ± 0.20that increased to 0.44 ± 0.23 after three months. Our results showed improvement of 2.50 ± 1.16 lines in the PBM group (P<.001) and 1.38 ± 0.72 lines in the control group (P=0.040). Our assessments showed no adverse related to the PBM in patients.

Conclusion: PBM facilitates and accelerates the occlusion therapy in amblyopia and it can be considered a treatment option for amblyopia.

Key Words: Amblyopia, PBM, Visual acuity, Occlusion therapy.

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INTRODUCTION

One of the most common causes of visual loss in children is amblyopia, which affects 2 to 3% of the pediatric population.[1] Different aspects of visual function including far and near visual acuity, contrast sensitivity, and binocular status are affected by amblyopia.[2] There are several treatments for amblyopia; optimal correction of refractive errors and occlusion of the dominant eye and forced use of the amblyopic eye are the most common methods.[3-4] Although, occlusion therapy is an effective treatment for amblyopia, but has some problems such as poor compliance, age at onset of therapy, type of amblyopia, and low motivation for occlusion therapy. These factors cause amblyopia therapy more difficult, especially in severe cases and in older children.[5-6] In recent years, other methods such as dichoptic training, perceptual learning, and video gaming have been presented that are based on active vision use. These methods showed improvement of visual acuity and stereopsis in amblyopia with good compliance.[7-10] One of the new therapies is based on Photobiomodulation (PBM), which was proposed by Ivandic and Ivandic. They used low-level lasers to treat adult patients with amblyopia. PBM treatment significantly improved visual acuity and increased multifocal VEP amplitude without adverse effects.[11]

In this regard, we designed our study to evaluate the therapeutic effects of PBM using LED device in amblyopia. Our goal in this study was to determine the efficacy and safety of 670 nm radiation and improvement of amblyopia in patients.

METHODS

This single-blinded, interventional study was performed after approval by the Human Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1399. 1279). Under the principles of Helsinki declaration and completed explanation of this study and treatment modality, the consent form was obtained from all participants.

This study was conducted on strabismus amblyopic patients in Abhar, Iran. Strabismus amblyopia was considered as an ocular misalignment of 10 prism diopter (PD) or more by alternate cover test and prism. The age range of our patients were from eight to thirteen years and there was no history of amblyopia therapy during past year or previously failed conventional treatments. They were divided into two groups: the PBM group and the control group. Our subjects were healthy and without ocular and systemic diseases.

We performed a comprehensive ophthalmic examination including best corrected visual acuity (BCVA) and strabismus measurement, objective and subjective measurement of refractive errors, slit lamp biomicroscopy, and fundoscopy. Best corrected visual acuity of the patients was measured by Snellen chart. Ocular alignment was evaluated by cover test in far and near distances and measured by prism bar. Objective refraction was determined by autorefractometer (Topcon Medical Systems, KR800) and retinoscopy (Beta 200 Heine, Germany), and verified by retinoscopy (Beta 200 Heine, Germany). Ocular health including anterior segment (eyelids, conjunctiva, cornea, anterior chamber, and lens) and posterior segment (vitreous, macula, retina, and optic nerve) of eyes was evaluated by an experienced ophthalmologist.

In the PBM group, PBM was performed on the amblyopic eye. For PBM, a portable device (Warp 10, Quantum device) was used by patients in their home. According to previous studies, we selected this device that was safe and showed no adverse effects of LED irradiation in human eyes.[11-12] The WARP 10 is a high intensity, hand-held, light emitting diode (LED) unit, emitted red light in the wavelength of 670 developing 25 Joules/cm2 energy at a distance of 3 cm. While the non-amblyopic eye was patched, the amblyopic eye was irradiated by red light of LED device for 240 seconds. After PBM, they did near activities such as playing digital game or drawing for 10 minutes. Patients had 3 sessions for a week that lasted for 3 months. Patients in the control group received conventional treatment. Patients did patching of non-amblyopic eye 2-3 hours daily for 3 months. During the patching time, patients performed near activities such as playing digital game or drawing. All patients were re-assessed 1, and 3 months after treatment.

Analysis of our data was performed by SPSS software version 18. After assessment of normal distribution of data with the Shapiro‑wilk test, we used kruskal-wallis, wilcoxon, and spearman's correlation tests.

RESULTS

There were 16 subjects (7 male and 9 female) with mean age of 9.88 ± 2.31 (range 8–13) years. The mean spherical equivalent was 4.50 ± 1.88 D with range of +1.00 to +7.50 D. All patients had strabismic amblyopia. Fourteen subjects were esotropic and two patients had exotropia. The mean size of strabismus was 19.69 ± 12.84 PD (5-45 PD). In the PBM group, the baseline best corrected visual acuity was 0.24 ± 0.15 and increased to 0.44 ± 0.26 and 0.49 ± 0.24 after one and three months of treatment respectively. In the control group, the mean BCVA was 0.30 ± 0.20 initially and increased to 0.40 ± 0.21 and 0.44 ± 0.23 in the first, and the third months post-treatment.

Our results showed improvement of 2.50 ± 1.16 lines in the PBM group (P<.001) and 1.38 ± 0.72 lines in the control group (P=0.040).Best corrected visual acuity improved to 1-2 lines in 7 patients and increased to 4 lines in one patient in the PBM group. In the control group, BCVA showed improvement of 1-2 lines in 6 patients and in 2 patients had no improvement.

Our results showed negative correlation between age and visual improvement in both groups (r= -0.395 and p= 0.130). In the PBM group, correlation between age and visual improvement was r= -0.272 and p= 0.514, and in the control group, this correlation was r= -0.519 and p= 0.187. Size of strabismus and visual improvement in both groups were related by r= -0.181 and p= 0.503.

During follow-up visits, patients in the PBM group were pleased and had good compliance to this method. In the second group, some patients were unhappy and said patching had affected their daily activities.Our assessments showed no adverse events such as blurred vision, increased intraocular pressure, and adverse events in anterior and posterior segments of patients in the PBM group.

Table 1: *Baseline characteristics of study patients.*

Type of treatment	PBM (n=8)	Occlusion (n=8)
Age(Y)	9.75± 2.18	9.99± 2.56
Spherical equivalent(D)	4.69± 1.71	4.37± 2.23
Strabismus(PD)	18.23± 15.20	16.50± 13.82
Baseline BCVA	0.24± 0.15	0.30± 0.20
First month BCVA	0.45± 0.25	0.40± 0.21
Third month BCVA	0.49±0.24	0.44.± 0.23
Improved BCVA(lines)	2.50±0.90	1.38±0.72
P	0.040	

DISCUSSION

Our results showed promising effects of 670 nm PBM in treatment of amblyopia. PBM before occlusion of amblyopic eye facilitated and accelerated the occlusion therapy in amblyopia. After three months, the average of visual acuity of patients improved 2.50 lines in the PBM group and 1.38 lines in the occlusion group. The rate of visual acuity improvement in the PBM group was nearly twice that of the occlusion group. While all of the patients in the PBM group had 1 or more lines improvement of visual acuity, 75% of patients in control group showed increased visual acuity. Although the rate of vision improvement decreased at older ages, there was no relationship between age and final vision. Patients in the PBM group were satisfied with this treatment and had good motivation for cooperation. But in the other group, patients had difficulties for occlusion of dominant eye. In agreement with our findings, Ivandic et al, used low level laser of 780 nm in adult amblyopic patients. After PBM, visual acuity of 89% of patients with strabismus improved 2.7 lines. The mean multifocal VEP amplitude increased and mean latency was reduced.[11]

In our view, the therapeutic effects of PBM for amblyopia have occurred by improving the function of retinal mitochondria and stimulating neural communication. Several studies have shown that retinal photoreceptors are the main target of PBM. Absorption of red to near-infrared light by mitochondria in photoreceptors results to promote mitochondrial membrane potential and ATP exchange, increased production of cytochrome oxidase, and reduced activity of cytochrome oxidase inhibitors.[12-13] In fact, PBM activates cytochrome C oxidase that has an essential role in the respiratory chain in mitochondria and down regulates inhibitory enzymes of cytochrome C oxidase. The enhancement of cytochrome C oxidase action improve metabolism and function of the cells.[14-16] In this regard, Grewal et al assessed therapeutic effects of670 nm light on healthy aging subjects.[17] Exposure to 670 nm light reduced rod-recovery time and increased scotopic thresholds. In another study by Shinhmar et al, exposure to red light in the morning in healthy subjects resulted in marked improvements in color contrast.[18]PBM promoted both tritan visual axis and protan visual axis due to enhanced mitochondrial performance in cones.[18] Finally, the mechanism of PBM is not exactly known and need more studies.

In assessments of PBM safety, our findings showed no adverse effects attributable to LED irradiation in our patients. Other studies demonstrated safety of PBM in ocular tissues and cells.[19-20]

Limitation of this study is the small sample size. We suggest further studies with more patients and more assessments with multifocal VEP and stereopsis tests.

CONCLUSION

In conclusion, PBM with 670 nm light showed promising results in amblyopia therapy without adverse effects. PBM with 670 nm light can be an adjunct treatment for conventional methods.

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Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(IR.SBMU.RETECH.REC.1399.1279).**

REFERENCES

1. **Chegeni M, Khanjani N, Rahmatpour P, Ahmadi Pishkuhi M, Abdolalian N.** The prevalence of amblyopia in Iran: A systematic review. J Curr Ophthalmol. 2018;**30(3):**194-201. Doi: 10.1016/j.joco.2018.02.003.
2. **Webber AL, Wood JM, Gole GA, Brown B.** The effect of amblyopia on fine motor skills in children. Invest Ophthalmol Vis Sci. 2008;**49(2):**594-603. Doi: 10.1167/iovs.07-0869.
3. **Papageorgiou E, Asproudis I, Maconachie G, Tsironi EE, Gottlob I.** The treatment of amblyopia: current practice and emerging trends. Graefes Arch Clin Exp Ophthalmol. 2019;**257(6):**1061-1078. Doi: 10.1007/s00417-019-04254-w.
4. **Suttle CM.** “Active treatments for amblyopia: a review of the methods and evidence base”. Clinical and Experimental Optometry 2010;**93:** 287-299. Doi: 10.1111/j.1444-0938.2010.00486.x
5. **Maconachie GD, Gottlob I.** The challenges of amblyopia treatment. Biomed J. 2015;**38(6):**510-516. Doi: 10.1016/j.bj.2015.06.001.
6. **Al-Zuhaibi S, Al-Harthi I, Cooymans P, Al-Busaidi A, Al-Farsi Y, Ganesh A.** Compliance of amblyopic patients with occlusion therapy: A pilot study. Oman J Ophthalmol. 2009;**2(2):**67-72. Doi: 10.4103/0974-620X.53035.
7. **Milla M, Piñero DP.** Characterization, passive and active treatment in strabismic amblyopia: a narrative review. Int J Ophthalmol. 2020;**13(7):**1132-1147. Doi: 10.18240/ijo.2020.07.18.
8. **Suttle CM.** Active treatments for amblyopia: a review of the methods and evidence base. Clin Exp Optom. 2010;**93(5):**287-299. Doi: 10.1111/j.1444-0938.2010.00486.x.
9. **Hernández-Rodríguez CJ, Piñero DP.** Active Vision Therapy for Anisometropic Amblyopia in Children: A Systematic Review. J Ophthalmol. 2020;**2020:**4282316. Doi: 10.1155/2020/4282316.
10. **Herbison N, MacKeith D, Vivian A, Purdy J, Fakis A, Ash IM, yet al.** Randomised controlled trial of video clips and interactive games to improve vision in children with amblyopia using the I-BiT system. Br J Ophthalmol. 2016;**100(11):**1511-1516. Doi: 10.1136/bjophthalmol-2015-307798.
11. **Ivandic BT, Ivandic T.** Low-level laser therapy improves visual acuity in adolescent and adult patients with amblyopia. Photomed Laser Surg. 2012;**30(3):**167-171. Doi: 10.1089/pho.2011.3089.
12. **Zhu Q, Xiao S, Hua Z, Yang D, Hu M, Zhu YT, et al.** Near Infrared (NIR) Light Therapy of Eye Diseases: A Review. Int J Med Sci. 2021;**18(1):**109-119. Doi: 10.7150/ijms.52980.
13. **Eells JT, Wong-Riley MT, VerHoeve J, Henry M, Buchman EV, Kane MP, et al.** Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy. Mitochondrion. 2004;**4(5-6):**559-567. Doi: 10.1016/j.mito.2004.07.033
14. **de Freitas LF, Hamblin MR.** Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. IEEE J Sel Top Quantum Electron. 2016;**22(3):**7000417. Doi: 10.1109/JSTQE.2016.2561201.
15. **Desmet KD, Paz DA, Corry JJ, Eells JT, Wong-Riley MT, Henry MM, et al.** Photomed Laser Surg. 2006;**24(2):**121-128. Doi: 10.1089/pho.2006.24.121.
16. **Fitzgerald M, Bartlett CA, Payne SC, Hart NS, Rodger J, Harvey AR, et al.** Near infrared light reduces oxidative stress and preserves function in CNS tissue vulnerable to secondary degeneration following partial transection of the optic nerve. J Neurotrauma. 2010;**27(11):**2107-2119. Doi: 10.1089/neu.2010.1426.
17. **Grewal MK, Sivapathasuntharam C, Chandra S, Gurudas S, Chong V, Bird A, et al.** A Pilot Study Evaluating the Effects of 670 nm Photobiomodulation in Healthy Ageing and Age-Related Macular Degeneration. J Clin Med. 2020;**9(4):**1001. Doi: 10.3390/jcm9041001.
18. **Shinhmar H, Grewal M, Sivaprasad S, Hogg C, Chong V, Neveu M, et al.** Optically Improved Mitochondrial Function Redeems Aged Human Visual Decline. J Gerontol A Biol Sci Med Sci. 2020;**75(9):**e49-e52. Doi: 10.1093/gerona/glaa155.
19. **Janis T Eells, Sandeep Gopalakrishnan, Thomas B Connor, Kimberly Stepien, Joseph Carroll, Vesper Williams, et al.** 670 nm Photobiomodulation as a Therapy for Diabetic Macular Edema: A Pilot Study. Invest. Ophthalmol. Vis. Sci.2017;**58(8):**932.
20. **Shen W, Teo KYC, Wood JPM, Vaze A, Chidlow G, Ao J, et al.** Preclinical and clinical studies of photobiomodulation therapy for macular oedema. Diabetologia. 2020;**63(9):**1900-1915. Doi: 10.1007/s00125-020-05189-2.

Authors’ Designation and Contribution

Masoumeh Ahadi; Student: *Concepts, Design, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Shahrokh Ramin; Associate Professor: *Concepts, Design, Data Acquisition, Data Analysis, Manuscript Editing, Manuscript Review.*

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