The effect of low-level laser therapy on visual function in glaucomatous patients.

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Abstract

Purpose: To evaluate the effect of ocular LLLT on structure and function in glaucomatous patients.
Methods: In this interventional case series, 12 eyes of 6 Iranian subjects were included. A diet rich in antioxidants was prescribed for all participants. LLLT was applied to the fovea, posterior pole, and occipital region. The regime of application of LLLT was 6 sessions every other day for 12 days, 30 days off, 3 sessions every other day for 6 days, 90 days off and finally 3 sessions every other day for 6 days. Evaluation of central 24 degrees of the visual field by Swedish Interactive Thresholding Algorithm (SITA), peripapillary Retinal Nerve Fiber Layer (RNFL), and macular ganglion cell complex (GCC) was done before and 4 months after the intervention.
Results: The mean age and intraocular pressure (IOP) were 54.8 ± 7.3 years and 15.9 ± 4.1 mmHg respectively. After treatment mean deviation (MD) of visual field improved from -6.25 dB (-24.48 to -0.1) (Median (Range)) to -2.78 dB (-21.5 to -0.18). There was no significant difference in the global RNFL and GCC thickness before and after the intervention.
Conclusion: LLLT can significantly improve the visual function of glaucomatous patients.

Keywords: Low Level Laser Therapy (LLLT), Glaucoma, Visual function.

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Introduction

Glaucoma is the second leading cause of blindness worldwide [1]. The prevalence and incidence of glaucoma are increasing because of a globally aging population [2]. The pathophysiology of glaucoma is not well understood yet but it is believed that increased intraocular pressure (IOP) would obstruct axoplasmic flow resulting in retinal ganglion cell death [3,4]. In many patients, glaucoma will progress despite achieving target IOP [5,6]. Other mechanisms such as mitochondrial dysfunction in retinal ganglion cells, impaired vascular supply, and the increased pressure gradient between intra ocular and intracerebral pressure have been proposed for the pathophysiology of glaucoma [7-10].

Because of the burden of disease treatment is an essential part of the management. IOP is the only modifiable risk factor and all the treatment options are focused on reducing IOP. In our era various medications and laser therapies are available and they prevent worsening of the disease in optimal settings. Although, Neuroprotective treatments have shown some success in the improvement of visual acuity in open-angle glaucoma (OAG) [11].

Due to increased IOP and ocular vascular compression, relative hypovolemia and hypoxia will occur resulting in mitochondrial oxidative stress and Retinal Ganglion Cell (RGC) death [12-15]. On the other hand, Low-Level Laser Therapy (LLLT) possibly affects Adenosine Triphosphate (ATP) production in mitochondria, modulation of oxidative stress, and induction of transcription factors [16-18].

Our goal in this interventional case series is to evaluate the effect of a diet rich in antioxidants and LLLT on the visual field in different types of glaucoma.

Materials and Methods

This interventional case series included 14 consecutive glaucomatous eyes of 6 Iranian subjects. There was one man and five women among our patients. The mean age ± SD was 54.8 ± 7.3 years. This study adhered to tenets of the Declaration of Helsinki and a written consent form was taken from all of the participants.

A thorough ophthalmic examination including Corrected Distance Visual Acuity, slit lamp examination, IOP measurement by Goldmann applanation tonometry, and funduscopy was done for each patient. Also, Optical Coherence Tomography (OCT) of the peripapillary Retinal Nerve Fiber Layer (RNFL) and macular ganglion cell complex (GCC) was taken for the entire participants before the intervention and 4 months after it. All patients underwent Standard Automated Perimetry C24-2 by the strategy of Swedish Interactive Thresholding Algorithm (SITA)-standard with a pattern like OCT. For basic data, two reliable perimetries were considered for each patient.

Besides routine antiglaucoma medication, our subject underwent LLLT and a diet rich in antioxidant was prescribed for them.

Diet

A no preserved extract of red fruits, nuts, saffron, and curcumin in the form of a sachet was given to each subject for daily use. They continued using this product for ninety days.

Low Level Laser Therapy (LLLT)

For LLLT we used light with a wavelength of 635-690 nm and 780 nm which are in the spectrum of red and infrared light, respectively. We applied it to the foveal region, posterior pole, and occipital region with a power of 300-800 μW, a diameter of 1 mm, and duration of 20 seconds (Lazar-ESL, Biomed Corp., Tehran, Iran). The regime of application of LLLT was 6 sessions every other day for 12 days, 30 days off, 3 sessions every other day for 6 days, 90 days off, and finally 3 sessions every other day for 6 days.

Statistical analysis

To present data we used mean, standard deviation, median and range, frequency and percentage. To compare the outcomes before and after the intervention we used the Wilcoxon signed-rank test. Besides, we report the 95% CI for the change of the parameters. All statistical analyses performed by SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). A p-value less than 0.05 considered statistically significant.

Results

The patients in our study had various types of glaucoma. Three patients had Primary Open Angle Glaucoma (POAG), two had Juvenile Open Angle Glaucoma (JOAG) and there was a patient with Primary Angle Closure Glaucoma (PACG) among our participants. Five patients were female (87.3%) and one patient (16.7%) was male. The mean ± SD age was 54.8 ± 7.3 years. The Mean ± SD IOP was 15.9 ± 4.1 mmHg on 3.08 ± 1.11 topical anti-glaucoma medications (Table 1).

Baseline characteristics		
Age	Mean ± SD	54.8 ± 7.3
	Median (range)	53 (48 to 67)
VA	Mean ± SD	0.03 ± 0.09
	Median (range)	0 (0 to 0.3)
SE	Mean ± SD	-0.41 ± 1.29
	Median (range)	-0.13 (-3.38 to 0.88)
IOP	Mean ± SD	15.9 ± 4.1
	Median (range)	15 (12 to 26)
Sex	Male	2 (16.7%)
	Female	10 (83.3%)
Glaucoma	POAG	6 (50.0%)
	PACG	2 (16.7%)
	JOAG	4 (33.3%)
Severity	Mild	6 (50.0%)
	Moderate	3 (25.0%)
	Advanced	3 (25.0%)
Laterality	OD	6 (50.0%)
	OS	6 (50.0%)
Number of anti-glaucoma medications	0	1 (8.3%)
	2	1 (8.3%)
	3	5 (41.7%)
	4	5 (41.7%)

Abbreviations: VA: Visual Acuity; SE: Spherical Equivalent; IOP: Intraocular Pressure; POAG: Primary Open-Angle Glaucoma; PACG: Primary Angle Closure Glaucoma; JOAG: Juvenile Open-Angle Glaucoma.

Table 1.*Baseline characteristics of the study eyes.*

After intervention including antioxidant therapy and LLLT mean deviation of the visual field improved from -8.47 ± 8.22 dB to -5.75 ± 6.6 dB (p=0.01). There was no statistically significant difference in average GCC or global RNFL thickness (Table 2).

		Mean ± SD	Median (range)	95% CI		p-value
				Lower	Upper	
MD	Pre	-8.47 ± 8.22	-6.25 (-24.48 to -0.1)			
	Post	-5.75 ± 6.6	-2.78 (-21.5 to -0.18)			
	Change	-2.72 ± 2.56	-2.76 (-8.68 to 0.8)	-4.35	-1.09	0.01
RNFL	Pre	80.75 ± 10.58	79 (67 to 101)			
	Post	80.08 ± 11.63	79 (62 to 101)			
	Change	0.67 ± 2.19	0.5 (-3 to 6)	-0.72	2.06	0.305
GCC	Pre	84.17 ± 9.25	83.5 (72 to 106)			
	Post	82.83 ± 9.6	81.5 (71 to 105)			
	Change	1.33 ± 1.15	1 (-1 to 3)	0.6	2.07	0.007

Abbreviations: MD: Mean Deviation; RNFL: Retinal Nerve Fiber Layer; GCC: Ganglion Cell Complex.

Table 2.*Function and structure before and after the intervention.*

Discussion

In this study, we showed the neuro-protective effects of LLL through improving the function of glaucomatous patients. After the invention of the ruby laser in 1960 and helium-neon laser in 1961, Low-Level Laser Therapy (LLLT) was first introduced by Endre Mester [19]. He noticed that low-level lasers fasten hair growth and wound healing in mice [20,21]. Red and near-infrared wavelengths are used in this therapy and

because of lower energy levels than conventional lasers they are called “low level” [19].

LLLT probably increases ATP production, modulates oxidative stress, and induces transcription factors [17,18]. Mitochondrial dysfunction and oxidative stress are the proposed mechanism for the progression of glaucoma. So, in this pilot study, our intention was to evaluate the effect of LLLT on various types of glaucoma.

Based on the literature we were expecting the stabilization of visual field, peripapillary RNFL, and macular ganglion cells in glaucomatous patients after LLLT. But surprisingly we were confronted by improving visual fields. Our explanation for this phenomenon is the cessation of the apoptotic process in retinal ganglion cells which are not working properly. These dying RGCs are responsible for the visual field defect and after LLLT they will come back to life and working properly. Also, a diet rich in antioxidants was prescribed for the patients and likely it has a synergistic effect on LLLT.

In a study by Jeffrey et al. was shown that applying pan macular Subthreshold Diode Micropulse laser (SDM) in eyes having POAG would improve mesopic visual acuity and P1 amplitude in visual evoked potential without any change in IOP. They attributed this improved visual function to the neuroprotective effects of the diode laser. Diode laser would reset the function of Retinal Pigment Epithelium (RPE) and tune the connections between RPE and inner retinal layers including RGCs [11].

Conclusion and Limitations

This study has several limitations. Lack of a control group and small sample size are the main shortcomings. Albeit, it should be said this was a pilot study. Future studies with a control group and a bigger sample size are recommended. In conclusion, we should say that considering LLLT in glaucomatous patients with deteriorating function could be a valuable option.

Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

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