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Effect of Transscleral Subthreshold Diode Laser Treatment to the Retinal Periphery in Glaucoma Patients (Photobiomodulation)

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ABSTRACT

Background: Reducing intraocular pressure (IOP) was only established method to limit rate at which damage progresses in glaucoma, a chronic, multifactorial optic neuropathy.

Objectives: This study aimed to determine how transscleral subthreshold diode laser treatment [photobiomodulation (PBM)] affects individuals with primary open angle glaucoma.

Subjects and methods: Ophthalmology departments, Clinics at Bab El-Shariyia University Hospital, El-Zahraa University Hospital in Cairo, Egypt, respectively, served as study's locations. Thirty eyes from nineteen individuals with primary open angle glaucoma, and a visual field impairment were included in this study.

Result: There was statistically significant improvement in the studied group regarding best-corrected visual acuity (BCVA) before and after intervention. There was highly statistically significance decrease in the intraocular pressure of patients before and after intervention in the studied group and significant improvement of visual field before and after intervention.

Conclusion: Micro pulse diode laser was a safe, efficient treatment for glaucoma, according to results of our study. BCVA and a highly statistically significant drop in intraocular pressure were outcomes of intervention. Visual field improved statistically significantly, as seen by decreases in mean deviation (MD), pattern standard deviation (PSD) prior to, and following intervention.

Keywords: Transscleral subthreshold diode laser, Retinal periphery, Glaucoma, hotobiomodulation.

INTRODUCTION

Degradation of optic nerve head (ONH) and retinal nerve fibre layer (RNFL) that was both progressive functionally. After light enters retina, photoreceptors transform it into electrical signals, which were then sent to brain via optic nerve. As glaucoma progresses, it results in blindness because it narrows field of vision by reducing number of optic nerve cells [1].

Age, ischaemia, structural factors were three primary causes of glaucoma. Age-assicated functional cell degradation raises incidence of glaucoma. High blood pressure or diabetes can cause ischaemia, which impairs optic nerve's ability to receive oxygen, nutrients that increases risk of injury. An increase in IOP was primary source of structural issues. It was referred either as primary-open angle glaucoma (POAG) or primary angle closure glaucoma (PACG) when it rises based on aetiology (Iris or trabecular meshwork). Normal-tension glaucoma (NTG) was a kind of glaucoma that can develop even when IOP was within normal range. Secondary glaucoma, which was brought on by other eye conditions such neovascularisation, uveitis, may be cause of NTG [2].

A number of factors contribute to rising incidence of glaucoma in young individuals, most notably rise in metabolic syndrome brought on by dietary changes in contemporary society. A person with metabolic syndrome has three or more metabolic problems, including high blood pressure, diabetes and high cholesterol [3].

Photobiomodulation (PBM) therapy was a new treatment for glaucoma that increases activity of Cytochrome C Oxidase (CCO), decreases oxidative stress, inflammation in eye, increases cell energy production, reduces ischemia-induced damage, lowers Glial Fibrillary Acidic Protein (GFAP), which was linked to stress response. Additionally, it enhances formation of antioxidants like vitamins C and E, which permanently lowers levels of reactive oxygen species (ROS) [2].

When living things were exposed to red light at the right intensity, oxidative stress, as well as inflammation were decreased, which promotes cell regeneration and quick tissue healing. Research on impact of PBM therapy indicates that it has a beneficial effect on repair of nerve tissue. Lack of efficient healing treatments and nerve lesions have significantly impacted people's lives [4].

Impact of photobiomodulation (PBM) therapy, which has garnered attention recently, offers crucial information for comprehending pathogenic process of glaucoma in relation to light wavelength for developing a treatment plan for condition. In its most basic form, PBM was used to biomodulate light photons. Wavelength range of near-infrared radiation is 780–940 nm. Low-level laser therapy (LLLT) was another name for PBM therapy [5]. PBM therapy was linked to effective nerve regeneration at cellular level through enhancing nutritional status, lowering inflammation, encouraging release of nerve factors. Consequently, PBM therapy offers a quicker, better

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recovery for peripheral nerve regeneration, repair as well as a reduction in inflammation, particularly in glaucoma, which was directly linked to loss of optic nerve [6].

Two main causes of glaucoma, ageing and IOP increase, which must be reduced in order to prevent and treat condition that makes eye vulnerable to subsequent damage. Consequently, PBM therapy was becoming a viable strategy for improving retinal ganglion cells' mitochondrial function, raising ATP synthesis [7].

Because it has a longer wavelength than other wavelengths, red light utilised in PBM therapy can penetrate dense tissues. It follows that therapeutic benefits of red light may now be used to treat retinal ganglion cells non-surgically, without requiring eye cuts. There was a higher chance of adverse consequences overall because medication interventions were applied directly to eyes. But since red light was absorbed as it travels across retina to produce therapeutic effects, there was little chance of adverse effects [8]. Therefore, this study aimed to assess impact of photobiomodulation, a transscleral subthreshold diode laser treatment, on cases with primary open angle glaucoma.

PATIENTS AND METHODS

At this prospective interventional non-randomized trial, thirty cases with primary open angle glaucoma who were seen at Outpatient Clinics of Bab-Elsheria University Hospital, Ophthalmology Department of El-Zahraa University Hospital were subjects. Cases privacy was protected by hiding all participant identities, substituting them with code numbers.

Inclusion criteria: Cases has glaucomatous visual field defect (thirty eyes), primary open angle glaucoma. Cases older than eighteen years.

Exclusion criteria: Ocular trauma history. History of laser treatment or eye surgery within last six months. Existence of additional retinal disorders, ex diabetic retinopathy. Individuals who couldn't follow up.

Each case in the study was subjected to the following: Detailed history taking from all cases, present, past medical history, history of ocular operation or trauma. Refractive errors measurement: Uncorrected distance visual acuity (UDVA).

Corrected distance visual acuity (CDVA).pa. Slit-lamp examination of anterior segment. Fundus examination using **volk+90 D lens (**ocular, U.S.A) on slit- lamp. **Optical coherence tomography** using **Topcon DRI OCT Triton** Topcon corporation, JAPAN) will be done on all cases for examination of optic nerve cupping, retinal nerve fiber layer thickness. **IOP** measurement by air puff (**Topcon** CT80 **non-contact tonometer** Topcon corporation, JAPAN), applanation tonometer. **Visual field** examination by Humphrey perimeter (**Heidelberg Engineering,** GmbH69121, Heidelberg, Germany).

Investigation: Visual field by Humphrey perimeter **(twenty-two)** pattern, SITA standad strategy (**Heidelberg Engineering**) (Figure 1).

Figure (1): Visual field will be conducted before first laser session and after every laser session.

Technique: TAHA technique is a new technique for treatment of diabetic retinopathy and glaucoma.

- ❖ We applied transconjunctival and transscleral sub threshold diode laser by slit lamp 7 mm from limbus.
- ❖ We focus on the sclera and defocus posteriorly to the retina and choroid.
- ❖ Laser shots were applied to the periphery of the retina up to the fornix.
- ❖ Laser shots were applied 360 degrees by the same way to the retinal periphery [9].

4-Treatment and follow up schedule:

Subthreshold micropulse laser was trans-scleral applied to the peripheral retina 7 mm from limbus. Laser treatment sessions were done using vitra 810 diode laser.

Fixed treatment parameters were used in all cases:

Laser aspect	specification
Size of laser sot	200 micro m
duration	200ms
Duty cycle	10%
Laser energy	500 mW
Wave length	810nm
Shots per session	300-500 shots
manufacturer	Vitra 810
Technique	Trans-scleral (TAHA technique)

SMPL treatment was performed every week for the first month and retreatment was performed every three weeks for six months if inadequate anatomical improvement was achieved. Follow up evaluation included BCVA measurement, visual field imaging and IOP measurment. In addition, treatment and retreatment were performed by the same doctor.

Ethical approval: This investigation received ethical clearance from The Research Ethics Committee, Ophthalmology Department, Faculty of Medicine, Al -Azhar University. All subjects provided written informed consents prior to their participation. The consent process included explicit information about data use and publication, with guarantees of privacy and confidentiality. The study conformed to the principles of the World Medical Association's Declaration of Helsinki.

Statistical analysis: Results were collected, tabulated, and statistically analysed by an IBM compatible personal computer with statistical package of the social sciences, version 20 (SPSS Inc. released 2011, IBM SPSS statistics for windows, version 20.0; IBM Corp., Armonk, New York, USA). Data were expressed as mean ± SD for continuous variables, and as percentages for categorical variables. Chi- squared test (χ^2) was used to check for significance and p value ≤ 0.05 was considered significant. Independent sample t test was applied to look for mean drain output before and after SK.

RESULTS

Table (1) showed that mean age of the studied patients was 51.36 ± 9.87 ranged from 38 to 70 years, 10 (33.3%) of patients were males while 9 (30%) of patients were females, 17 (56.7%) of patients had right side affection, 13 (43.3%) of patients had left side affection and mean CCT of the studied patients was 529.8 ± 15.4

Table (1): Distribution of cases characteristics in studied group

	Studied group (N=30 eyes)
Age (years)	
Mean ± SD (Range)	51.36 ± 9.87 (38-70)
Sex	
Male	10 (33.3%)
Female	9 (30%)
Side	
Right	17 (56.7%)
Left	13 (43.3%)
CCT	
Mean ± SD	529.8 ± 15.4

CCT: Central Corneal Thickness.

Table (2) showed that 1 (3.3%) patient had hypertension, 1 (3.3%) was cardiac patient, 3 (10%) of patients had asthma, 3 (10%) of patients had bilateral phaco + IOL surgery, 2 (6.7%) of patients had bilateral phaco+ IOL, 1 (3.3%) of patient had phaco-trab surgery and 18 (60%) of patients were on BB + CAI and 12 (40%) of patients were on BB + CAI + alpha 2 agonist.

Table (2): Distribution of medical history in the studied group

	Studied group (N=30 eyes)
Past medical history	
Hypertension	1 (3.3%)
cardiac patients	1 (3.3%)
Asthma	3 (10%)
Past surgical history	
Bilateral phaco + IOL	5 (6.7%)
phaco-trab	1 (3.3%)
Glaucoma treatment	
BB+CAI	18(60%)
BB+CAI+alpa2agonist	12(40%)

BB: beta blocker, CAI: carbonic anhydrase inhibitor

Table (3) showed that there was statistically significance improvement in studied group regarding BCVA before and after intervention.

Table (3): Distribution of BCVA before, and after intervention in studied group

	Studied group (N=30 eyes)		
	Before	**After**	**P value**
BCVA	0.48± 0.45	0.3±0.25	0.04

P value >0.05: Not significant, P value <0.05 is statistically significant, p<0.001 is highly significant. SD: standard deviation, BCVA: Best-corrected visual acuity.

Table (4) showed that there was no statistically significant difference in studied group regarding RNFLT and C/D ratio before & after intervention.

Table (4): Distribution of OCT before, and after intervention in studied group

	Studied group (N=30 eyes)		
RNFLT	**Before**	**After**	**P value**
Mean± SD	66.06±20.4	70.13±20.84	0.447
C/D ratio			
Mean± SD	0.71±0.167	0.68±0.16	0.480

RNFLT: retinal nerve fiber layer thickness, C/D ratio: cup-to-disc ratio.

Table (5) showed that there was statistically significant improvement in the visual field before and after intervention with statistically significant improvement in MD and PSD before and after intervention.

Table (5): Distribution of visual field before, and after intervention in studied group

	Studied group (N=30 eyes)			
	At baseline	**After 1 month**	**At final**	**P value**
Reduction				
mild	13 (43.3%)	18 (60%)	19 (63.3%)	0.574
marked	11 (36.7%)	9 (30%)	9 (30%)	
moderate	5 (16.7%)	2 (6.7%)	1 (3.3%)	
severe	1 (3.3%)	1 (3.3%)	1 (3.3%)	
MD				
Mean± SD	-13.8 ±9.39	-9.83 ± 6.92	-8.5±7.8	**0.035**
PSD				
Mean± SD	+6.34 ±2.03	+5.4±2.20	+4.86±2.40	**0.036**

Table (6) showed that there was highly statistically significant decrease in the intraocular pressure of patients before and after intervention in the studied group.

Table (6): Distribution of IOP before and after intervention in the studied group

	Studied group (N=30 eyes)			
	At baseline	**After 1 month**	**At final**	**P value**
IOP				
Mean± SD	18 ± 2.37	16.3±1.88	15.33±2.18	<0.001

DISCUSSION

Only known method to limit rate of damage progression in glaucoma, a chronic, multifactorial visual neuropathy, was to lower IOP. Surgical techniques were necessary to achieve desired IOP when medicinal or laser therapies were ineffective. Regretfully, a large number of cases may not respond well to common surgical techniques, leading to repeated failures [10].

Impact of photobiomodulation (PBM) therapy, which has garnered attention recently, offers crucial information for comprehending pathogenic process of glaucoma in relation to light wavelength, for developing a treatment plan for condition. In its most basic form, PBM was used to biomodulate light photons. Wavelength range of near-infrared radiation was 780–940 nm. Low-level laser therapy (LLLT) was another name for PBM therapy [5].

Growth factor release, transcriptional activation of cytokine expression, upregulation of matrix metalloproteinases occur when accumulation of denatured proteins reaches threshold of sub-lethal cellular injury [11].

Several biochemical mediators with anti-angiogenic properties, including pigment epithelium derived growth factor (PEDGF), can be upregulated by it. Additionally, micropulse laser treatment promotes production of substances that raise angiotensin II, receptor activation, which allows VEGF (vascular endothelial growth factor) to be inhibited. Vascular permeability was decreased by decrease in VEGF [12].

This study aimed to evaluate the effect of transscleral subthreshold diode laser treatment to retinal periphery in primary open angle glaucoma patients (photobiomodulation). This study was conducted in Ophthalmology Department Clinic of El-Zahraa University Hospital, Cairo, Egypt and Ophthalmology Department, Clinic of Bab el-Shariyia University Hospital, Cairo, Egypt. The study included (thirty eyes) of cases with primary open angle glaucoma and visual field defect.

Our results showed that mean age of the studied patients was 51.36 ± 9.87 ranged from 38 to 70 years, 10 (33.3%) of patients were males while 9 (30%) of patients were females, 17 (56.7%) of patients had right side affection, 13 (43.3%) of patients had left side affection and mean CCT of the studied patients was 529.8 ± 15.4. Our findings are consistent with those of **Luttrull *et al.*** [13] who discovered that eighty eight eyes from forty eight consecutive cases remained for investigation after 1 cases (One eye) was lost to follow-up before postoperative testing. These were twenty man, twenty-eight woman, ages fifty seven to ninty four (Average age: seventy nine). Range of IOPs on topical medicines was zero-three (Average: 1.6) to six-twenty three mmHg (Average: thirteen). Systemic glaucoma treatment was not used by any. Before, majority of cases had undergone laser trabeculoplasty.

Three of eyes previously had anterior chamber shunt implanted or had a trabeculectomy.

Our results showed that 1 (3.3%) of patient had hypertension, 1 (3.3%) was cardiac patient, 3 (10%) of patients had asthma, 5 (16.7%) of patients had bilateral phaco + IOL surgery, 1 (3.3%) of patient had phaco-trab surgery and the majority of patients 18 (60%) took dual therapy BB + CAIED for Glaucoma treatment, 12 (40%**)** took triple therapy BB + CAI + alpha 2 agonist ED. Our results showed that there was statistically significance difference in studied group regarding BCVA before and after intervention (p =.04). Our findings are consistent with those of **Siqueira *et al.*** [14] who demonstrated a noteworthy improvement in BCVA, with an average drop from 1.1 to 0.98 LogMAR (p = 0.01). Upon visual field analysis, mean deviation (12.6% to 10.6%), standard deviation (10.54% to 9.89%) and index of deviation (fifty six percent to sixty percent) of background perimeter, all showed significant improvements (p = 0.02, 0.03 and 0.02 respectively). OCT, ERG results showed no abnormalities, no adverse events were reported throughout the follow-up period.

Our results showed that there was no statistically significance difference in the studied group regarding RNFLT and C/D ratio before and after intervention (p value >.05). Our results showed that there was statistically significance improvement in the visual field before and after intervention with reduction of MD (P = 0.035) and PSD before and after intervention (p = 0.036). Our findings concur with those of **Luttrull *et al.*** [15] who discovered that eighty eight eyes belonging to forty eight cases (twenty man and twenty eight woman) distanced between fifty seven, ninty four years of age (avg. 79). Before SDM, all cases experienced glaucomatous optic nerve cupping & visual field loss. IOPs on 0-3 (avg. 1.6) medicines ranged from six to twenty three mmHg (avg. 13). They had performed significant glaucoma surgery on thirty three eyes. Visual acuities before SDM ranged from twenty/fifteen to count fingers (median twenty/sixty). VA and IOP remained unaffected after SDM. VEP P1 amplitudes increased considerably (p=0.001). Following SDM, there was a significant improvement in visual area by ORP, global macular acuity (an average of logMAR acuities within ten degrees of fixation, or GMA), best logMAR visual acuities with six degrees of fixation (BA6) (p<0.0001, p=0.003 & p<0.0001 respectively).

Luttrull *et al.* [15] discovered that increases in optic nerve function coincided with significant improvements in mesopic visual function. All gains were made without reducing IOP or causing side effects. These findings show that panmacular SDM could be 1st therapeutically beneficial neuroprotective therapy for OAG that can enhance visual function and fields without lowering IOP. Our findings differ from those of **Agnifili *et al.*** [16]**,** who observed no difference in baseline VF damage across groups, with MD values of -14.81 ± 1.21 dB and -15.23 ± 1.15 dB in Ss and Fs respectively (p > 0.05). At latest follow-up, MD did not significantly alter in Ss or Fs (−15.07 ± 1.24 dB and −15.39 ± 1.16 dB, respectively).

Taha *et al.* [9] reported that transscleral micropulse diode laser treatment of diabetic macular oedema and proliferative diabetic retinopathy (TAHA Technique) is an easy new technique, effective and safe treatment way.

Surprisingly our results showed that there was highly statistically significant decrease in the intraocular pressure of patients before and after intervention in the studied group. As photobiomodulation increases uveoscleral out flow and so decrease IOP. Because laser beam hits non-secreting region of CB, AH transport failure was unlikely to be sole (or primary) mechanism of action used by MP-TLT to reduce IOP [17]. Histological studies on enucleated cadaver eyes, which evaluated tissue effects of MP-TLT, continuous-wave (CW)-TSCPC, found that breakdown of secretive CB epithelium was produced by CW-TSCPC but not by MP-TLT [18]. Our findings align with **Ahn *et al.*** [2] who discovered that laser intervention altered mean IOP. While there was no significant difference in IOP before intervention (P = 0.117). Significant differences were observed at thirty minutes, four weeks post-treatment between groups (P < 0.001 at both time points). Our findings are consistent with **Gull *et al.*** [19] who discovered a significant drop in IOP from baseline at each follow-up. Average pre-laser, post-laser corrected visual acuity was 0.06 ± 0.17 Snellen decimal. Nine eyes experienced early moderate post-laser inflammation, three had early hypotony & tonic pupil, two had IOP spikes and one eye developed corneal oedema and hyphaema. Treatment effectiveness was observed in fifty one (eighty five percent) cases after three months, forty eight (eighty percent) at six months. Use of antiglaucoma drugs significantly decreased from 3.85 ± 0.10 to 1.07 ± 0.16 (p = 0.000). **Barac *et al.*** [20] discovered that successful MP-TLT resulted in a 7.3% increase in choroidal thickness that persisted until third month. Post-treatment increases in gaps between ciliary muscle bundles were observed. All of these findings suggest that MP-TLT may have little effect on AH inflow, an increase in outflow could be a main mechanism for decreasing IOP.

LIMITATIONS

Short term follow-up and limited number of cases, therefor longer follow up period and larger number of patients may be required to provide more robust conclusions.

CONCLUSION

We concluded that micropulse diode laser is safe and effective treatment for glaucoma patients. There was highly statistically significant decrease in the intraocular pressure and statically significant improvement in BCVA of patients before and after intervention. Also, we concluded that there was statistically significance improvement in the visual field before and after intervention at Reduction of MD and PSD before and after intervention.

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