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ORIGINAL ARTICLE

CHANGES IN RETINAL NERVE FIBER LAYER THICKNESS ON HEIDELBERG RETINAL TOMOGRAPHY IN PATIENTS OF PRIMARY OPEN ANGLE GLAUCOMA AFTER TRABECULECTOMY VERSUS ANTI GLAUCOMA MEDICATION

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ABSTRACT

OBJECTIVE: To compare the retinal nerve fiber layer (RNFL) thickness changes in patients of primary open-angle glaucoma after trabeculectomy versus anti-glaucoma medication.

METHODS: This quasi-experimental study was conducted from 10th February, 2017 to 28th February, 2018 on 60 patients presenting to the Institute of Ophthalmology, Mayo Hospital, Lahore, Pakistan using non-probability consecutive sampling. Patients were assigned to two equal groups: group A (n=30) patients underwent trabeculectomy while group B (n=30) patients were put on anti-glaucoma medication. Pre-treatment and three months post-treatment RNFL thickness was recorded and then analyzed using SPPSv.18.0.

RESULTS: Out of 60 patients, Group A (n=30) had 14 (46.71%) males and 16 (53.31%) females, while Group B (n=30) had 16 (53.31%) males and 14 (46.71%) females. The mean age was 55.901±4.221 and 55.431±3.971 years in Group A and Group B respectively (p=0.661). In age group, 16 (53.31%) each in Group A and Group B were <55 years. Hypertensive status showed 9 (30.01%) and 5 (16.71%) hypertensive patients in Group A and Group B respectively. Mean change in RNFL thickness was 0.028±0.012µ and 0.013±0.007µ in Group A and Group B respectively (p=<0.001). Pre and post-treatment (pre:post) RNFL thickness (µ) in males, females, hypertensive, non-hypertensive, age <55 years, and age ≥55 years was 0.201±0.175µ:0.226±0.155, 0.205±0.159:0.233±0.019, 0.193±0.015:0.223±0.013, 0.206±0.015:0.233±0.018, 0.208±0.015:0.232±0.021, and 0.196±0.016:0.228±0.015 for Group A and 0.211±0.018:0.224±0.019, 0.201±0.015:0.215±0.014, 0.214±0.015:0.226±0.016, 0.205±0.018:0.218±0.017, 0.206±0.017:0.219±0.015, and 0.209±0.019:0.221±0.020 for group B respectively.

CONCLUSION: Trabeculectomy increases thickness of retinal nerve fiber layer more than anti glaucoma medication.

KEY WORDS: Retina (MeSH); Glaucoma, Open-Angle (MeSH); Trabeculectomy (MeSH); Nerve Fibers (MeSH); Heidelberg Retinal Tomography (Non-MeSH).

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INTRODUCTION

Glaucoma is an irreversible and progressive optic neuropathy causing structural changes to the optic nerve head (ONH) and retinal nerve fiber layer (RNFL) along with loss of visual field, the most important risk factor for which is raised Intraocular pressure (IOP).[1,2] RNFL changes always precede changes in ONH parameters and visual field defects.[3] One of the most important cause of permanent blindness around the globe is glaucoma.

The pooled global prevalence of primary open angle glaucoma (POAG) is estimated to be 3.54%.[4] In addition, Asia account for 53.4% of worldwide POAG cases.[5]Glaucoma damage once done is permanent, it cannot be reversed. The end point of managing glaucoma is to help prevent the further loss of RNFL. Using medication, IOP is lowered either by reducing the amount of fluid produced in the eye or by increasing the aqueous outflow. The aim of treatment is to preserve the visual field function and reduce the IOP which is enough to achieve a therapeutic goal termed the 'target IOP range'.[6]Target IOP is the range of IOP on therapy that will prevent further damage and visual field loss without affecting patient's quality of life.[7]Trabeculectomy is the surgical procedure for lowering IOP, advised when IOP remains uncontrolled by maximally tolerated anti-glaucoma therapy. Since its advent, new advancements have been made in this surgery regarding site of surgery, limbus versus fornix based flap, use of post-operative steroids, releasable sutures, argon laser suture lysis, needling and use of antimetabolites.[8]Ganglion cell loss is estimated to be 40% to 50% in glaucoma before the measurements reaches statistical significance.[9] RNFL analysis provides an alternative to the visual inspection of the optic nerve, neuro-retinal rim as well as a

TABLE I: DISTRIBUTION ACCORDING TO AGE, GENDER, HYPERTENSION AND RNFL THICKNESS IN BOTH GROUPS

Parameter		Group A n=30	Group B n=30	P-Value
Age (years)		55.901±4.221	55.431±3.971	0.661**
Mean Change in RNFL* Thickness (μ)		0.028±0.012	0.013±0.007	< 0.001**
Gender	Male	14 (46.67%)	16 (53.33%)	0.606***
	Female	16 (53.33%)	14 (46.67%)	
Hypertensive Status	Hypertensive	9 (30%)	5 (16.67%)	0.222***
	Non-Hypertensive	21 (70 %)	25 (83.33%)	
Age Group (years)	< 55	16 (53.33%)	16 (53.33%)	0.999***
	≥55	14 (46.67%)	14 (46.67%)	

*Retinal Nerve Fiber Layer, **Independent sample T-test. *** Chi-Square's test*

quantitative estimation of retinal ganglion cell axonal loss.[10] Two most important tools are optical coherence tomography (OCT) and Heidelberg retinal tomography (HRT).[11,12] The HRT is a 3D confocal scanning laser ophthalmoscope non-invasive procedure which scans retina in 24 milliseconds 64 consecutive sequential scans, starting above the retinal surface, and then capturing parallel images at increasing depths 0-4mm over an area of 15 degree using 670ηm diode laser.[13]

Absence of any local literature on possible effects of glaucoma treatment modalities on RNFL and varying results in international literature was the rationale to conduct this study. The objective of this study was to compare the possible effects of anti-glaucoma medication and trabeculectomy on the thickness of RNFL as measured on HRT in patients of primary open-angle glaucoma.

METHODS

This quasi-experimental study was conducted from 10th February, 2017 to 28th February, 2018 after obtaining ethical approval from the Institutional Review Board of King Edward Medical University, Lahore, Pakistan. Patients presenting to the outpatient department of Mayo Hospital, Lahore were screened for inclusion and exclusion criteria. Patients (n=60) between 40-70 years of age and diagnosed with primary open angle glaucoma at various stages requiring surgical or augmentation of medical therapy were selected by non-probability consecutive sampling. Patients who were diagnosed with secondary glaucoma or any coexisting ocular pathology except for refractive errors were excluded from study. Demographic data of patients was recorded and pre-treatment RNFL thickness was measured on HRT. Among all 60 patients, 30 were assigned as Group A patients and underwent trabeculectomy while 30 were put in group B, which were put on anti-glaucoma medication. Post treatment retinal nerve fiber layer thickness was measured on HRT after three months and findings recorded on proforma. In trabeculectomy, a fistula was created between anterior chamber of eye and subtenon space facilitating the flow of aqueous and reducing intra ocular pressure. Group B patients were started on double agent anti-glaucoma medication (Dorzolamide HCl & Timolol Maleate eye drops, twice daily). The data was entered and analyzed in SPSS v.18.0. The quantitative data like age and pre and post treatment retinal nerve fiber layer thickness were presented as mean and standard deviation. The qualitative data like gender was presented as frequency and percentage. Independent sample T test was applied for comparison of mean retinal nerve thickness change in both study groups, Paired Sample T-test was used for comparison of pre- and post-treatment RNFL thickness and Chi-Square was applied for categorical variables, p-value ≤0.05 was considered significant.

RESULTS

The mean age of patients in group A was 55.901±4.221 years and in group B it was 55.431±3.971 years. In group A, mean change in RNFL thickness on HRT was 0.028±0.012 microns while in group B it was 0.013±0.007 microns (Table I).

In group A, mean change in RNFL thickness in male patients was 0.026±0.011 microns and in female patients it was 0.029±0.013 microns (p=0.595). Mean change in RNFL thickness in hypertensive patients was 0.030±0.012 microns while it was 0.027±0.012 microns in non-

TABLE II: CHANGE IN RETINAL NERVE FIBER LAYER THICKNESS IN BOTH GROUPS

Variable		Group A n = 30		Group B n = 30	
		Mean Change in RNFL* Thickness (μ)	P-Value	Mean Change in RNFL* Thickness (μ)	P-Value
Gender	Male (n=30)	0.026±0.011	0.595	0.013±0.007	0.661
	Female (n=30)	0.029±0.013		0.014±0.006	
Hypertensive Status	Hypertensive (n=14)	0.030±0.012	0.482	0.012±0.008	0.714
	Non-Hypertensive (n=46)	0.027±0.012		0.013±0.006	
Age Group (years)	<55 (n=30)	0.024±0.013	0.047	0.013±0.007	0.913
	≥55 (n=30)	0.032±0.009		0.013±0.006	

*Retinal Nerve Fiber Layer; **Independent sample T-test.*

TABLE III: PRE AND POST-OPERATIVE RETINAL NERVE FIBER LAYER THICKNESS PROFILES IN BOTH GROUPS

Variable	Group A (n=30)			Group B (n=30)		
	Pre-Treatment RNFL* Thickness (μ)	Post-Treatment RNFL* Thickness (μ)	P-value**	Pre-Treatment RNFL* Thickness (μ)	Post-Treatment RNFL* Thickness (μ)	P-value**
Male (n=30)	0.201±0.175	0.226±0.155	<0.001	0.211±0.018	0.224± 0.019	<0.001
Female (n=30)	0.205±0.159	0.233±0.019	<0.001	0.201±0.015	0.215± 0.014	<0.001
Hypertensive (n=14)	0.193±0.015	0.223±0.013	<0.001	0.214±0.015	0.226±0.016	0.099
Non-Hypertensive (n=46)	0.206±0.015	0.233±0.018	<0.001	0.205±0.018	0.218±0.017	<0.001
Aged below 55 Years (n=30)	0.208±0.015	0.232±0.021	<0.001	0.206±0.017	0.219±0.015	<0.001
Aged 55 Years or above (n=30)	0.196±0.016	0.228±0.015	<0.001	0.209±0.019	0.221±0.020	<0.001

*Retinal Nerve Fiber Layer; **Paired Sample T-test*

hypertensive patients (p=0.482). The mean change in RNFL thickness in those aging below 55 years was 0.024±0.013 microns and it was 0.032±0.009 microns in those aging 55 years or above (Table II). In group B, mean change in RNFL thickness was 0.013±0.007 microns in male patients while it was 0.014±0.006 microns in female patients (p=0.661). In hypertensive patients, mean change in RNFL thickness in hypertensive patients was 0.012±0.008 microns while in non-hypertensive patients it was 0.013±0.006 microns (p=0.714). Mean change in RNFL thickness in those younger than 55 years was 0.013±0.007 microns while it was 0.013±0.006 microns in those aging ≥55 years (p=0.913) (Table II). The pre- and post-treatment RNFL thickness in both groups as per gender, hypertensive status and age group has been explained in Table III.

DISCUSSION

The above results showed that retinal nerve fiber layer thickness increases in response to treatment of glaucoma whether surgical or medical. However, the increase in retinal nerve fiber layer thickness was more in patients who underwent trabeculectomy as compared to those who were on anti-glaucoma medications. The increase in thickness of retinal nerve fiber layer was almost double in trabeculectomy group as compared to anti-glaucoma medication group. The increase in retinal nerve finer layer thickness was also observed in all sub groups i.e. male and female patients, hypertensive and non- hypertensive patients, patients aging 55 years or above and below 55 years of age.

Raghu N et al[14] have studied the effect of filtration surgery on thickness of retinal nerve fiber layer. They studied 11 patients pre- and post-trabeculectomy. They documented a significant increase in average (p=0.019) and inferior (p=0.038) RNFL thickness after one week of surgery only to decrease back to pre-operative level after 3 months. However our study showed an increase in RNFL thickness at 3 months. Maneesang S, et al.[15] have studied the RNFL thickness changes pre and 3 months post filtration surgery for lowering the intraocular pressure. In their study 19 patients were included in whom the average RNFL thickness decreased from 59.58±17.59 microns to 57.19±14.97 microns contrary to our study. The thickness in four quadrants did not change significantly.

In a study,[16] researchers evaluated the changes in RNFL after lowering of intra ocular pressure either by medical or surgical means. They selected 21 patients and followed them before and after the glaucoma treatment. In their study, lowering the intra ocular pressure either medically or surgically did not affect the average RNFL thickness. Quadrant analysis also showed no noticeable change in RNFL thickness in all four quadrants.

Park and associates[17] have studied the short term behavior of retinal nerve fiber layer on Heidelberg retinal tomography after glaucoma filtration surgery. They studied 13 eyes of 13 patients pre operatively and two months post operatively on Heidelberg retinal tomography. They noted that mean retinal nerve fiber layer thickness in those patients increased from 0.135±0.129 microns preoperatively to 0.162±0.091 microns after two months of surgery. The results of this study were synonymous with our research although the followup period was more in our study.

Yamada and colleagues[18] used scanning laser polarimetry to evaluate the changes in retinal nerve fiber layer after glaucoma filteration surgery. They selected 46 eyes of 46 patients who had undergone uneventful filteration surgery resulting greater than 30% reduction of intra ocular pressure. They concluded that postoperatively the retinal nerve fiber layer thickness increased in superotemporal and inferotemporal regions and this increase was statistically significant (P<0.05). Present study also showed a statistically significant increase in RNFL thickness after surgical therapy.

In a study,[19] researchers have studied the retinal nerve fiber layer changes on optical coherence tomography after trabeculectomy. They noted a statistically significant increase in retinal nerve fiber layer thickness after trabeculectomy (P<0.0001). This study showed similar results to above mentioned research although no comparisons with medical therapy were made. Quadrant wise analysis also showed a significant elevation in retinal nerve fiber layer thickness in superior, temporal and nasal segments.

Koraszewska-Matuszeuska and associates[20] have studied the changes in retinal nerve fiber layer inpatients of

juvenile glaucoma after filtration surgery for lowering the intra ocular pressure. In their study, average RNFL thickness increased from 60.61 microns to 63.09 microns after surgery. Also average superior half thickness increased from 74.14 microns to 78.33 microns and in inferior half it increased from 70.54 microns to 72.42 microns. Though this study was conducted on patients of juvenile glaucoma in contrast to our study population of adult onset glaucoma, the results are strikingly aligned.

Rebolleda G[21] studied the changes in retinal nerve fiber layer thickness after deep sclerectomy for lowering the intra ocular pressure. They did not found any statistically significant changes in RNFL after sclerectomy.

Our study sample size was 60 with a single followup at 3 months which is small enough to make conclusive recommendations on the effects of glaucoma therapy on thickness of retinal nerve fiber layer. However, it gives an idea on which large randomized controlled trials with longer duration and multiple follow-ups can be based for a better understanding.

CONCLUSION

Surgical management (trabeculectomy) leads to more increase in retinal nerve fiber layer thickness as compared to medical therapy.

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AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

AR: Conception and study design, acquisition of data, drafting the manuscript, final approval of the version to be published

AAK: Acquisition of data, critical review, final approval of the version to be published

MS: Analysis and interpretation of data, drafting the manuscript, final approval of the version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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