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RETINAL GANGLION CELL COMPLEX CHANGES ON OPTICAL COHERENCE TOMOGRAPHY AFTER PANRETINAL PHOTOCOAGULATION FOR TREATMENT OF PROLIFERATIVE DIABETIC RETINOPATHY

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ABSTRACT

Objective: To study the changes in ganglion cell complex as measured on Optical coherence tomography after panretinal photocoagulation for the treatment of diabetic retinopathy.

Study Design: Quasi experimental study.

Place and Duration of Study: Department of Ophthalmology, Lahore General Hospital, Lahore from Apr 2017 to May 2018.

Methodology: Patients presenting to the Eye Out-patient department Lahore General Hospital were assessed for inclusion and exclusion criteria. All patients (n=38) diagnosed with proliferative diabetic retinopathy requiring panretinal photocoagulation were included in study. Retinal ganglion cell complex thickness was measured in superior, inferior, superonasal, supero-temporal, inferonasal and inferotemporal quadrants. besides that signal strength on Optical coherence tomography was also documented. Pre-operatively, visual acuity was measured and Optical coherence tomography performed and the findings were recorded on a designed proforma. Post-operatively, the patients were called for follow-up after one monthand three months at which time Visual acuity was again measured and Optical coherence tomography performed and findings recorded in the proforma. All the lasers were performed by single surgeon.

Results: The thickness of ganglion cell complex decreased from 83.18 ± 3.83µm to 80.55 ± 3.58µm three months after panretinal photocoagulation. The decrease in ganglion cell complex thickness was statistically significant (p<0.001).

Conclusion: Panretinal photocoagulation leads to a decrease in thickness of retinal ganglion cell complex on optical coherence tomography.

Keywords: Ganglion cell complex, Optical coherence tomography, Panretinal photocoagulation.

INTRODUCTION

Diabetes mellitus is one of the major endocrine morbidities around the world[1]. It affects all vital systems of the body such as kidneys, liver, heart, central nervous system and the eyes. The most common ocular manifestation of diabetes mellitus is the involvement of retinal blood vessels called diabetic retinopathy. In diabetic retinopathy, Retinal blood vessels undergo changes which ultimately lead to the formation of new fragile blood vessels without structural supporting elements called the proliferative diabetic retinopathy[2]. Proliferative diabetic retinopathy results from poor long term glycemic control and is more common in young type 1 diabetics as compared to type 2 diabetics[3]. Complications of proliferative diabetic retinopathy include vitreous hemorrhage and tractional detachment which may lead to permanent visual loss if not treated promptly[4]. Diabetic retinopathy is affected by various factors such as dyslipidemias, pregnancy, uncontrolled blood pressure and status of renal function[5-7]. Treatment of proliferative diabetic retinopathy is aimed at controlling the advancing stage of diabetic retinopathy and also at preserving the vision from permanent damage. Proliferative diabetic retinopathy is characterized by increased levels of Vascular Endothelial growth factors secreted by ischemic retina which predispose the formation of neovessels[8]. The standard treatment for the treatment of diabetic

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retinopathy is panretinal photocoagulation[9]. In this laser procedure Argon laser is applied to the peripheral retina in order to convert from ischemic retina to dead retina. The dead retinal tissue does not produce vascular endothelial growth factor thus halting the progression of proliferative diabetic retinopathy and its subsequent complications[10]. Ganglion cell complex comprises of two vital layers of retina i.e. ganglion cell layer and inner plexiform layer. The thickness of ganglion cell complex is important in relation to the development and progression of glaucoma. This complex also serves as a tool to monitor the progression of disease and the effect of its treatment. Thus this layer assumes critical importance as it may be affected by various ocular diseases and interventions (Laser for proliferative diabetic retinopathy). Optical coherence tomography (OCT) is a diagnostic modality which is non-invasive and is used to capture three dimensional scans of all the layers of retina and also in the study of anterior segment structures. It captures micro resolution images so it gives an excellent details of individual details of al retinal layers by mapping the ultrastructural anatomy.

METHODOLOGY

This quasi experimental study was conducted at Lahore General Hospital from April, 2017 to May, 2018 after obtaining approval from the Ethical Review Committee of Hospital. To calculate sample size, authors used power analysis on G-power statistical software version 3.1. By using paired samples t-test and assumed "Temporal" as an outcome variable. Enter the required information mean and standard deviation of temporal at baseline was 85.4 ± 16.1 and temporal after 3 months was 91.2 ± 15.1and calculated effect size and power (1-β) was 0.471 and 0.80 respectively[14]. As a result a total 38 samples was required to justify the effect of study parameters.

Patients (n=38) were selected by non-probability consecutive sampling who were diagnosed with proliferative diabetic retinopathy on slit lamp fundus examination, requiring panretinal photocoagulation. Patient diagnosed with any co existing ocular disease such as retinal detachment, vitreous hemorrhage, visually significant cataract hindering OCT measurement and corneal or any other media opacity were excluded from study. Patients were counselled about the stage of diabetic retinopathy and negative impact on vision if not treated. Informed consent was obtained from all patients before performing laser. Prelaser ganglion cell complex thickness was measured along with signal strength on OCT and documented on the proforma. After aseptic measure, pupils were pharmacologically dilated in the eye to be lased. Laser was applied on slit lamp laser delivery system. 2000-2500 burns were applied using a spot size of 200 microns, pulse duration of 100 milliseconds and 250-300 milli Watt of power. Post-laser patients were prescribed antibiotic eye drops four times daily for one week and NASID tablet three times daily for one week. Patients were called for followup after one and three months at which time OCT was again performed to measure and document the thickness of ganglion cell complex and signal strength.

Data was entered and analyzed using SPSS version 22. Frequencies and percentages were calculated for categorical variables while mean and standard deviation were calculated for numerical variables. Visual acuity between pre-PRP and post -PRP was assessed by McNemer's test. The difference between Pre-Laser and Post-Laser treatment (Pre-Laser, 1 month Post-Laser and 3 month Post-Laser) was determined by repeated measures ANOVA and Post Hoc Test. Statistical significance was defined as p-value of ≤0.05.

RESULTS

This study included 38 patients of proliferative diabetic retinopathy who underwent pan retinal photocoagulation and showed a reduction in ganglion cell complex thickness after one and three months of laser. Mean age of patients was 60.66 ± 5.51 years. Of the 38 patients, 23 were male (60.5%) and 15 (39.5%) were female. Panretinal photocoagulation was performed in left eyes of 16 (42.1%) patients and right eyes of 22 (57.9%) patients (table-I). Pre-PRP visual acuity

was 6/36 in 10 (26.3%) and 6/60 in 28 (73.7%) patients as measured on Snellen's chart. Three months post-PRP visual acuity was 6/36 in 12 (31.6%) patients and it was 6/60 in 26 (68.4%) patients as measured on Snellen's chart. The change in visual acuity was not statistically significant (p 0.804) (table-II). Pre-PRP, the mean geographical ganglion cell complex thickness was 83.18 ± 3.83 which was reduced to 82.53 ± 3.75 at one month post-PRP and to 80.55 ± 3.58 at three months post-PRP. The mean Sup-erior ganglion cell complex thickness was 83.18 ± 3.42 and at one month post-PRP it was 82.24 ± 3.32 which further reduced to 79.97 ± 3.23 after three months of PRP. The mean inferior ganglion cell complex thickness pre-PRP was 82.03 ± 3.02 and it was 81.42 ± 2.96 and at three months post-PRP it was 79.16 ± 2.85. Pre-PRP, mean superonasal ganglion cell complex thickness was 82.87 ± 3.13 which reduced after one month of PRP to 82.03 ± 2.99 and further reduced to 80.11 ± 2.91 at three months post-PRP. The mean superotemporal ganglion cell complex thickness pre-PRP was 81.47 ± 2.25 which was 80.55 ± 2.15 at one month post-PRP and further reduced to 78.61 ± 2.10 after three months of PRP. Pre-PRP, mean infero-nasal ganglion cell complex thickness was 81.13 ± 2.33 which reduced to 80.32 ± 2.19 at one month Post-PRP and further reduced to 78.45 ± 2.29 after three months of PRP. Mean inferotemporal ganglion cell complex thickness pre-PRP was 81.13 ± 2.13 which after one month of PRP was reduced to 80.26 ± 1.95 and later on further reduced to 78.32 ± 1.89 at three months after PRP. The thickness of ganglion cell complex was measured in microns and the reduction in thickness post-PRP was statistically significant (p<0.001). The signal strength on OCT pre-PRP was 8.26 ± 0.69, at one month Post-PRP it was 8.66 ± 0.48 and it was 8.55 ± 0.50 after three months of PRP (p 0.009) (table-III).

Table-I: Age, Gender and Laterality of patients.

Parameter	Mean ± SD
Age in Years*	60.66 ± 5.51
Frequency (%)	
Gender	
Male	23 (60.5)
Female	15 (39.5)
Eye	
Left	16 (42.1)
Right	22 (57.9)

Table-II: Changes in Visual Acuity of patients.

Visual Acuity	Pre-PRP	3 month Post-PRP	p value
6/36	10 (26.3%)	12 (31.6%)	0.804
6/60	28 (73.7%)	26 (68.4%)	

p-value was calculated by McNemer Test

Continuous variables were presented as Mean ± Standard deviation. p: Repeated measures ANOVA test was applied. Bonferroni Post Hoc Test was applied: p* (pre-PRP versus 1 month post-PRP), p** (pre-PRP versus 3 months post-PRP), p*** (1 month Post-PRP versus 3 month Post PRP).

Table-III: Changes in Ganglion Cell Complex Thickness.

Parameter	Pre-PRP n=38	1 Month Post-PRP n=38	3 Month Post-PRP n=38	p-value	p* value	p** value	p*** value
Total	83.18 ± 3.83	82.53 ± 3.75	80.55 ± 3.58	<0.001	0.041	0.043	0.023
Superior	83.18 ± 3.42	82.24 ± 3.32	79.97 ± 3.23	<0.001	0.034	0.035	0.025
Inferior	82.03 ± 3.02	81.42 ± 2.96	79.16 ± 2.85	<0.001	0.032	0.031	<0.001
Supero-Nasal	82.87 ± 3.13	82.03 ± 2.99	80.11 ± 2.91	<0.001	0.032	0.011	0.044
Supero-Temporal	81.47 ± 2.25	80.55 ± 2.15	78.61 ± 2.10	<0.001	0.034	0.012	0.046
Infero-Nasal	81.13 ± 2.33	80.32 ± 2.19	78.45 ± 2.29	<0.001	0.041	0.023	0.011
Infero-Temporal	81.13 ± 2.13	80.26 ± 1.95	78.32 ± 1.89	<0.001	0.044	0.011	<0.001
Signal Strength	8.26 ± 0.69	8.66 ± 0.48	8.55 ± 0.50	0.009	0.003	0.163	0.999

DISCUSSION

The authors present the changes in ganglion cell complex thickness after panretinal photoco-

agulation for the treatment of proliferative diabetic retinopathy. The study found a reduction in thickness of retinal ganglion cell complex in geographical as well as in all the six quadrants after panretinal photocoagulation. The signal strength also changed on OCT after one and three months of panretinal photocoagulation but it was not statistically significant. During literature search, various studies were found assessing the effects of ocular surgery on the thickness of retinal ganglion cell complex[11-15]. Absence of local literature was the rationale to conduct this study to see the effects on local population. Hollo *et al* have compared the measurement of ganglion cell complex between two software versions (6.3 & 6.12) of RTVue-100 OCT. The ganglion cell complex thickness values did not differ between the two softwares both before and after surgery. However, The ganglion cell complex thickness increased after surgery as measured by both soft wares but the increase documented by software version 6.12 was statistically significant ($p<$ 0.0001). Neither focal loss volume (FLV) nor global loss volume (GLV) differed between the software versions before and after surgery[15]. Perdicchi A and colleagues have studied changes in ganglion cell complex changes after treatment of age related macular degeneration with intravitreal ranibizumab. Their study showed a decrease in thickness of 8.1 ± 20.2µm after a single injection of intravitreal ranibizumab. this decrease in retinal ganglion cell complex thickness was statistically significant although the visual acuity and central macular thickness were reduced. But they were not sure if repeated intravitreal injections of anti VEGF progressively decrease the ganglion cell complex thickness[16]. Baba *et al* have studied the changes in ganglion cell complex thickness after internal limiting membrane peeling during vitrectomy for macular hole. They noted a decrease in thickness of ganglion cell complex from 95.5 ± 6.8 microns to 84.9 ± 10.0 at three months and 84.2 ± 10.8 at six months after surgery. This decrease in ganglion cell complex thickness both at three and six months was statistically significant[17]. Rimayanti *et al* have studied ganglion cell complex and retinal nerve fiber layer changes in patients with neovascular age related macular degeneration as compared to patients with dry age related macular degeneration and glaucoma. They have found different ganglion cell complex values in normal subjects and those with both dry and wet age related macular degeneration with glaucoma and correlated with disease severity[18]. Esin *et al* have compared the effect of intracameral anes-thesia on ganglion cell complex after uneventful phacoemulsification surgery. They divided the patients into two groups. One group received preservative free 1% lidocaine while the other group received sham balanced salt solution at the end of uneventful phacoemulsification surgery. post operatively, Both groups showed increase in ganglion cell complex thickness at one week and at one month ($p<0.001$)[19]. Lee *et al* have studied the changes in retinal ganglion cell complex thickness after treatment of central retinal vein occlusion with intravitreal anti-VEGF agents. The have found a significant decrease in retinal ganglion cell complex thickness after multiple injections of intravitreal anti-VEGF. This change in thickness correlated with central macular thickness and number of injections[20]. Eun *et al* have studied ganglion cell complex thickness changes after epiretinal membrane surgery. In this study the post-operative ganglion cell complex thickness was compared with the fellow normal eye after six months. The ganglion cell complex thickness was significantly lower in eyes which underwent surgery i.e. 71.77 ± 10.21 as compared to the nor-mal fellow eyes i.e. 81.69 ± 5.33 microns[21]. Bonin *et al* have studied the retinal ganglion cell complex changes in eyes with resolved diabetic macular edema and compared it to those without any diabetic macular edema. In their study they found that average retinal ganglion cell complex thickness in eyes with diabetic macular edema was 74 ± 14 microns as compared to 83.2 ± 6 microns in eyes without diabetic macular edema. This difference in retina; ganglion cell complex thickness was statistically significant[22]. Dorothy *et al* have studied the changes in retinal ganglion cell complex and retinal

nerve fiber layer in patients with diabetic retinopathy as compared to controls. They concluded that retinal ganglion cell complex thickness in patients with diabetic retinopathy was 4.49 microns less than those controls without diabetic retinopathy[23].

CONCLUSION

Retinal ganglion cell thickness was reduced in our study both after one and three months of pan retinal photocoagulation for the treatment of proliferative diabetic retinopathy. The reduction in thickness was statistically significant. The authors recommend large randomized controlled trials with a longer followup period to have a better knowledge of effects of panretinal photocoagulation on retinal ganglion cell complex.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Zimmet P, Alberti AG, Magliano DJ, Bennet PH. Diabetes mellitus statistics on prevalence and mortality: Facts and fallacies. Nature Reviews Endocrinol 2016; 12(10): 616-22.
2. Nentwich MM, Ulbig MW Diabetic retinopathy-Ocular complications of diabetes mellitus. World J Diabetes 2015; 6(3): 489-99.
3. American Diabetes Association. Standards of medical care I diabetes-2015 abridged for primary care providers. Clin Diabetes 2015; 33(2): 97-11.
4. Meleth A, Carvounis PE. Outcomes of vitrectomy for tractional retinal detachment in diabetic retinopathy. Int Ophthalmol Clin 2014; 54(2): 127-39.
5. Das R, Kerr R, Chakarvarthy U, Hogg RE. Dyslipidemia and diabetic and macular edema: A systematic review and meta-analysis. Ophthalmol 2015; 122(9): 1820-27.
6. Morrison JL, Hodgson LAB. Diabetic retinopathy in pregnancy: a review. Clin Exp Ophthalmol 2016; 44(4): 321-34.
7. Sabanayagam C, Yip WF, Ting DSW, Tan G, Wong TY. Ten emerging trends in the epidemiology of diabetic retinopathy. Ophthal Epidemiol 2016; 23(4): 209-22.
8. Rahimy E, Shahlaee A, Khan MA, Ying GS, Maguire JI. Conversion to Aflibercept after prior anti-VEGF therapy for persistent diabetic macular edema. Am J Ophthalmol 2016; 164(1): 118-27.
9. Okamoto M, Matsuura T, Ogata N. Effects of panretinal photocoagulation on choroidal thickness and choroidal blood flow in patients with severe non-proliferative diabetic retino-pathy. Retina 2016; 36(4): 805-11.
10. Chawla A, Chawla R, Jaggi S. Microvascular and macrovascular complications in diabetes mellitus: Distinct of continuum?. Indian J Endocrinol Metab 2016; 20(4): 546-51.
11. Fortune B, Cull G, Reynaud J, Wang L. Relating retinal ganglion cell function and retinal nerve fiber layer retardance to progressive loss of RNFL thickness and optic nerve axons in experimental glaucoma. Invest Ophthalmol Vis Sci 2015; 56(6): 3936-44.
12. Banitt MR, Ventura LM, Feuer WJ, Savatovsky E, Luna G, Shiff O, et al. Progressive loss of retinal ganglion cell function pre-cedes structural loss by several years in glaucoma suspects. Invest Ophthalmol Vis Sci 2013; 54(3): 2346-52.
13. Hwang TS, Gao SS, Liu L, Lauer AK. Automated quantification of capillary non-perfusion using optical coherence tomography angiography in diabetic retino-pathy 2016; 134(4): 367-73.
14. Lee SB, Kwag JY, Lee HJ, Jo YJ, Kim JY. The longitudinal changes of retinal nerve fiber layer thickness after pan retinal photocoagulation in diabetic retinopathy patients. Retina 2013; 33(1): 188-93.
15. Hollo G, Nagizadeh F, Hsu S, Filkorn T, Bausz M. Comparison of the current and a new RTVue OCT software version for detection of ganglion cell complex changes due to cataract surgery. Int Ophthalmol 2015; 35(6): 861-67.
16. Perdicchi A, Peluso G, Iacovello D, Balestrieri M, Fave MD et al. Ganglion cell complex evaluation in exudative age related macular degeneration after repeated intravitreal injections of Ranibizumab. Biomed Res Int 2015; 2015(1): 268796-02.
17. Baba T, Yamamoto S, Kimoto R. Reduction of thickness of ganglion cell complex after internal limiting mem-brane peeling during vitrectomy for idiopathic macular hole. Eye 2012; 26(9): 1173-80.
18. Rimayanti U, Kiuchi Y, Yamane K, Latief MA. Inner retinal layer comparisons of eyes with exudative age related macular degeneration and eyes with age related macular degeneration and glaucoma. Graefe's Arc Clin Experiment Ophthalmol 2014; 252(4): 563-70.
19. Sari ES, Ermis SS, Yazici A, Koytak A, Sahin G, Kilic A. The effect of intra cameral anesthesia on macular thickness and ganglion cell-inner plexiform layer thickness after uneventful hacoemulsification surgery: prospective and randomized control trial. Graefe's Archive Clin Experiment Ophthalmol 2014; 252(3): 433-39.
20. Lee JY, Kim HC. Ganglion Cell Layer thickness after Anti-Vascular endothelial growth factor treatment in retinal vein occlusion. J Korean Ophthalmol Soc 2016; 57(1): 63-70.
21. Lee EK, Yu HG. Ganglion cell-inner plexiform layer thickness after epiretinal membrane surgery. Ophthalmol 2014; 121(8): 1579-87.
22. Bonin S, Tadayoni R. Correlation between ganglion cell layer thinning and poor visual function after resolution of diabetic macular edema. Invest Ophthalmol & Vis Sci 2015; 56(2): 978-82.
23. Dorothy SK, Peggy PC, Gavin T, Cheung G, Cheng CY. Retinal ganglion cell neuronal damage in diabetes and diabetic retinopathy. Clin Exp Ophthalmol 2016; 44(4): 243-50.