Analysis of peripapillary choroidal thickness in primary open angle glaucoma.

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Abstract

To assess the effect of Silicone Oil (SO) tamponade on Best-Corrected Visual Acuity (BCVA) when used in macula-on Retinal Detachments (RD). Methods: Retrospective, non-randomised interventional case series of consecutive patients with macula-on RD where SO was successfully used to reattach the retina. The following variables were analysed: hospital site, gender, age, axial length, pre-operative BCVA, presence of vitreous haemorrhage, giant retinal tear, or proliferative vitreoretinopathy, lens status during SO tamponade, duration of SO tamponade, use of perfluorcarbon liquid, an encircling band and the illumination source during Removal of SO (ROSO). The main outcome measure was BCVA at 3 months after ROSO.

Keywords: Antioxidants, Reactive oxygen species, Anticarcinogenicity, Antimutagenicity, Antiallergenicity.

Introduction

Glaucoma is the second leading cause of blindness worldwide. It is estimated that primary open angle glaucoma (POAG), by far the most common type of glaucoma, will affect 79.76 million people aged 40- 80 years by 2040. The underlying mechanism of POAG is still unclear. Although increased intraocular pressure (IOP) is the main risk factor, multiple studies have shown that reduced perfusion to optic nerve head (ONH) may have a role in development and progression of open angle glaucoma (OAG) [1].

Choroid is a highly vascular layer which supplies most of the blood flow of the retina and prelaminar part of ONH. Yin ZQ et al and Spraul et al reported decreased and increased choroidal thickness in patients having POAG by histologic studies, respectively. Postmortem changes and processing artifacts may affect the morphology of choroid in such studies. Imaging technologies such as fluorescein angiography and laser Doppler flowmetry which don't have these drawbacks also have shown delayed and decreased blood flow to ONH [2].

Newer imaging methods like enhanced depth imaging (EDI) and swept source (SS) optical coherence tomography (OCT) have provided high resolution in vivo cross-sectional images of choroid. Recent studies have applied these methods for measurement of choroidal thickness (CT) in peripapillary (PP) and macular regions of glaucoma patients. These studies including two meta-analysis had mixed results. According to the mixed results of previous studies, The purpose of this study is to compare our goal in this study was comparing peripapillary PPCT in POAG and healthy control eyes using EDI- OCT [3].

Methods

In this observational cross-sectional study 61 eyes of 54 patients having POAG and 37 eyes of 34 healthy subjects were enrolled. Eyes in the POAG group were recruited among newly diagnosed patients of glaucoma clinic of Farabi Eye Hospital and eyes in the control group were chosen among healthy volunteers. Tenets of declaration of Helsinki were adhered in this study and ethics committee approval of Tehran University of Medical Sciences was granted [4] (Table 1).

Patients

All eyes underwent thorough and comprehensive ophthalmic examination including, measurement of best corrected distance visual acuity,(CDVA), slit-lamp biomicroscopy, tonometry by Goldmann applanationtonometry, gonioscopy, dilated funduscopy, measurement of the central corneal thickness (CCT)by pachymetry (Tomey Corporation, Nagoya, Japan) and ocular biometry (IOLMaster; Carl Zeiss Meditec).Also, aAchromatic standard automated perimetry using central 24-2 Swedish Interactive Threshold Algorithm (Humphrey VisualField Analyzer; Carl Zeiss-Meditec

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Inc., Dublin, CA) and circumpapillary RNFL scanning byHeidelberg Spectralis OCT (Heidelberg Engineering, Inc., Dossenheim, Germany)were performed in all eyes [5].

Table 1: The eyes in POAG group had thinner RNFL globally (70 ± 14 µm vs. 95.4 ± 8.7 µm) and in superotemporal (88 ± 22.9 µm vs. 122.4 ± 18.6 µm), superonasal (77.8 ± 25.6 µm vs. 111.4 ± 21.9 µm), nasal (57 ± 14.6 µm vs. 77.8 ± 11 µm), inferonasal (79.5 ± 23.1 µm vs. 118.7 ± 20.3 µm) and inferotemporal (86 ± 29.7 µm vs. 132 ± 17.6 µm) sectors (P < 0.001). RNFL thickness in temporal sector was not significantly different between POAG and control groups (58.3 ± 14.8 µm vs. 61.4 ± 11.4 µm) (P= 0.277)

	Control Group	POAG Group	P value
No (eye)	34(37)	54(61)	
Age(years)	69.1 ± 6.4	68.6 ± 10.8	0.827
Gender(M/F)	17/20	40/41	0.056
Refractive error [SE] (D)	0.1 ± 1.5	0.2 ± 1.4	0.873
IOP (mmHg)	13.5 ± 2.6	17.6 ± 6.9	<0.001
CCT (µm)	536.2 ± 43.6	537.1 ± 39.1	0.935
Axial length (mm)	23.3 ± 0.8	23.5 ± 0.9	0.385
Visual field MD (dB)	0.2 ± 1.3	-7.8 ± 6.4	<0.001
D: diopter; IOP: intraocular pressure; CCT: central corneal thickness; MD: mean deviation, SE: spherical equivalent			

EDI SD-OCT

All eyes in this study underwent peripapillary retinal nerve fiber layer (cp-RNFL) scanning by Heidelberg Spectralis SD-OCT (Heidelberg Engineering; Spectralis software version 5.3.2) after pupillary dilation. Peripapillary pp-RNFL thickness measurements were done by using a circle with diameter of 3.5 mm centered on ONH. Images with quality score < 20, uneven illumination, poor centration and segmentation excluded from analysis. Images in which the posterior border of choroid was not delineable were also excluded [6].

Measurement of choroidal thickness

For measurement of choroidal thickness, the choroid in B-scan which is represented as a strip by the device was manually outlined. The inner and outer boundaries were outlined at the base of retinal pigment epithelium (RPE) and choroidoscleral junction, respectively. Choroidoscleral junction is a hyper reflective layer between large vessels of the choroid and sclera (Figure 1). The measurements were done by Heidelberg Eye Explorer software (HEYEX™ Heidelberg Engineering, Dossenheim, Germany) globally and in temporal, superotemporal, superonasal, nasal, inferonasal, inferotemporal sectors [7].

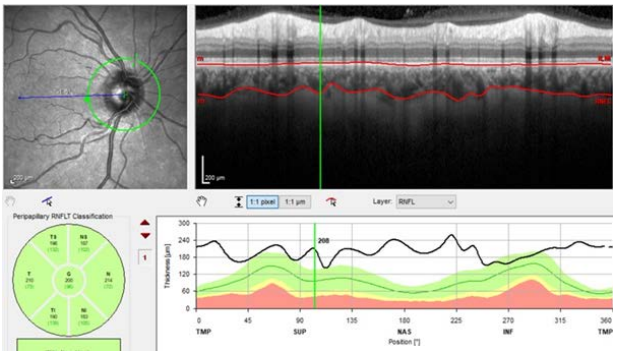

Figure 1: Choroidoscleral junction is a hyperreflective layer between large vessels of the choroid and sclera.

Statistical analysis

The distribution of numerical data was tested for normality using the Shapiro-Wilk test. For comparing parametric and non-parametric variables student's t test or Mann-Whitney U test were applied respectively. Categorical variables were compared by chi square test. Student's t test was used to compare patient level demographic continuous variables between POAG andPOAG and glaucoma subjects. Categorical variables were compared using Fisher's exact test. Mixed-effects models were used to compare ocular parameters between groups. Models were fit with ocular measurements as dependent variables and diagnostic group as a fixed effect. Eye level measurements were nested within subject to account for the fact that eyes from the same individual are more likely to have similar measurements. (reference)Momodels for choroidal thickness were adjusted for To adjusting age, sex and axial length. for choroidal thickness, linear mixed modeling was used [8].

Results

The correlation between choroidal thickness and patient factors was assessed by Pearson correlation analysis univariate linear mixed model was used to explore the factors that are associated with choroidal thickness. Multivariable models was were built to adjust for age, gender, axial length and factors with P<0.15 in univariable model. Given the collinearity of the visual field MD and RNFL, separate models were fitted and the coefficients of association for each model were reported. Statistical analyses were performed using STATA v. 15.0 (StataCorp, College Station, TX). The alpha level (type I error) was set at 0.05 [9].

Discussion

Various studies have shown that factors other than IOP

may have a role in pathophysiology of POAG. One of these factors is disturbed blood supply to the ONH that can lead to development and progression of glaucomatous optic neuropathy. Choroid is a highly vascularized tissue and is responsible for perfusion of optic nerve specially in the prelaminar region. Histologic assessment of choroid in patients having POAG are contradictory and have found increased or decreased CT in comparison to age- matched healthy subjects. This contradiction may be related to postmortem changes and processing artifacts. Also studies that have applied imaging modalities like radiofrequency, doppler flowmetry and flourscein angiography have mixed results. By using EDI function of SD-OCT, CT could be measured in detailed cross sectional images of choroid [10].

In our study eyes in POAG group had lower CT globally and in all sectors except nasal sector. As previous studies have shown CT decreases by increasing age and axial length. Gender comparison had a borderline significance in categorical analysis. So, after controlling age, gender and axial length, eyes in POAG group had lower CT globally and in temporal, superotemporal and inferotemporal sectors. Interestingly, this finding supports vascular theory of POAG and is in concordance with glaucoma tendency to damage neuroretinal rim in supero- and inferotemporal sectors.

Previous studies have applied different methods and imaging modalities for measurement of peripapillary PPCT. Ehrlich et al, Maul et al and Park et al found no difference in peripapillary PPCT between OAG and normal subjects or OAG suspects. But there are multiple studies which have shown thinner peripapillary PPCT in OAG or normal tension glaucoma (NTG) [11].

Komma et al in a study evaluated peripapillary PP and macular CT by SD-OCT and swept source OCT (SS-OCT) in normal and POAG subjects. In measurements that were done by SD-OCT in their study, there was no significant difference in peripapillary PPCT between POAG and normal eyes. But when measurements were done by SS-OCT, POAG eyes had thicker peripapillary PPCT in all quadrants except inferior quadrant. They attributed this finding to medications and reduced IOP in treated patients. But the IOP reduction in glaucomatous patients didn't result in greater CT in inferior qudrant. We also showed a lower CT in supero- and inferotemporal sectors, which are common locations for glaucomatous damage. So, the results of our studies confirms each other [12].

As previous studies have shown similar to previous investigations, in our the present study there was a negative correlation between age and global CT in univariate regression analysis but there was no significant correlation between axial length and global peripapillary PPCT, probably because of low standard deviation and low dispersion of axial lengths. In the two multivariable models that were constructed by controlling for age and gender, visual field MD and global RNFL thickness were positively correlated with global CT. This finding means that more functional or structural damage in POAG is in correlation with lower peripapillary PPCT [13].

Roberts et al compared peripapillary PPCT between healthy controls and patients with Focal, Diffuse, and Sclerotic Glaucomatous Optic Disc Damage. They found a negative correlation between sclerotic ONH damage and peripapillary PPCT in OAG (POAG, pseudoexfoliative and pigmentory glaucoma) (-41 μm; 95% CI, -59 to -23 μm; P.001). Although the correlation between peripapillary PPCT and focal or diffuse ONH damage was not significant, their study showed a correlation between particular type of structural damage and peripapillary PPCT [14].

Our study has several limitations. First, we used EDI SD-OCT as imaging modality. In this imaging system inner and outer boundaries of choroid could be unclear and difficult to outline. SS-OCT systems can provide better visualization of choroidoscleral junction and applying this system for measurement of CT should be more accurate. Second, this study had a cross sectional desing and precedence of CT change or ONH damage could not be detected. Third, because of small sample size we didn't categorize POAG eyes according to severity. So, we suggest future studies with larger sample size, prospective design and newer imaging techniques for evaluation of the role of choroid in glaucoma [15, 16].

Conclusion

Our study showed that, In conclusion, the present study demonestrated that in eyes having POAG,PPCT peripapillary CT is significantly lower in temporal, superotemporal and inferotemporal sectors regionally and globally in POAG eyes compared to healthy controls. Older age and more severe glaucoma were as associated with thinner choroid in these eyes. Based on anatomical measurements, the choroid seems to be significantly altered in POAG patients in Iranian population. Future studies investigating the choroidal vascular flow are indicated to confirm the role of the choroid in the pathophysiology of open-angle glaucoma and more functional or structural damage is in correlation with lower PPCT.

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