www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i5.173

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Corneal Endothelial Cell Changes in POAG & Its Relation with Severity of Field Defect

Authors
Dr Prasannakumary.C, Dr Ragi. T K, Dr Raju K V
GMCH, Kozhikode
Email: *prakuharitham@gmail.com, Mobile: 9447636451*

Abstract

Introduction: *The corneal endothelium is a single layer of polygonal cells covering the posterior surface of Descemet's membrane. The endothelial cells have the lowest mitotic activity. The corneal endothelium regulates hydration of cornea through ATP and biocarbonate-dependent pump and thereby providing transparency. In the adult, the average cell density is 2600 - 3000 cells/mm^2.[1] Glaucoma is an optic neuropathy characterized by progressive loss of retinal ganglion cells, thinning of the neuroretinal rim and the retinal nerve fiber layer (RNFL), with associated deterioration of the visual field.[3] It can cause defects to the corneal endothelial cells either by direct or indirect mechanisms.*

Aim: *The aim was to compare corneal endothelial cell changes among Primary open angle glaucoma patients and normal control group and to correlate endothelial changes with duration of disease and severity of field defects.*

Methods: *It is a cross sectional comparative study comprised of 200 eyes, each of POAG patients and of normal individuals of similar age group who attended the outpatient department. Corneal endothelial cells were examined using noncontact specular microscope.*

Results: *The mean endothelial cell density (ECD) in POAG patients were significantly lower (2211.13 ± 171.49cells/mm^2 in right eye, 2198.20± 154.39cells/mm^2 in left eye) compared to control group (2417.43 ± 116.92 in right eye and 2390.18 ±101.31 cells/mm^2 in left eye, p value <.001). Hexagonality in POAG patients also were significantly less. (43.79 ±5.77, 43.58± 6.82 in right and left eye respectively as to control group 48.25± 2.82, 48.71± 2.89 ,p value <.001). Coefficient of variation in POAG patients was significantly higher than control group.*

Conclusion: *Corneal Endothelial cell density and percentage of hexagonal cells were significantly lower among Primary open angle glaucoma patients. Evaluation of corneal endothelium is necessary for proceeding to intraocular procedures in glaucoma patients.*

Keywords: *Open angle glaucoma, endothelial cell density, Hexogonality, coefficient of variation.*

Materials and Methods

This is a cross sectional comparative study done on two hundred eyes each of POAG and controls of same age group. Cases were selected from the patients under treatment for primary open angle glaucoma in the outpatient Department from January 2014 to December 2015. The informed consent and ethical committee approval obtained. The inclusion criteria was diagnosed cases of Primary open angle glaucoma with the following findings. 1. Evidence of glaucomatous damage as determined by the appearance of optic nerve head. 2.Gonioscopic evidence of open angles 3.Baseline IOP more than 21mm of Hg as determined by applanation tonometry 4.Abnormal results in at least 2 consecutive visual field examinations as defined by the Anderson's criteria. Controls were patients of similar age group attending the ophthalmology OPD with diseases other than glaucoma in whom: IOP less than 21 mm of Hg, normal visual field and normal optic disc appearance. Patients having history of chronic ocular inflammation, ocular surgery, corneal diseases, ocular trauma, contact lens wear, and systemic illness such as diabetes mellitus, chronic renal disease were excluded. All patients diagnosed to have POAG after slit lamp examination, intraocular pressure measurement using Goldmann applanation tonometer, fundus examination using direct and indirect ophthalmoscopy, 90D lens, gonioscopy, visual field examination using Humphrey's field Analyser (HFA) were examined for endothelial cell count. Corneal endothelial measurement was done using specular microscope (TOPCON model SP 3000P non-contact specular microscope). An average of 3 readings of the endothelial counts in the central corneal quadrants was taken in to account. 80 cells were counted with the variable frame analysis by centre cell counting method. Statistical analysis was performed using SPSS after entering the data in excel sheet. Each eye was considered separately while doing analysis.

Results

A total of 200 eyes of POAG patients and 200 eyes of control intividuals were included in the study. Among them 91 were males and 109 were females. The age group of study individuals was between 40 – 70 years.As shown in Fig.1, there was a significant reduction in endothelial cell density (ECD) and hexagonality (HX) (p value <0.01) and increase in coefficient of variation (CV) in both cases and control groups as age increases.

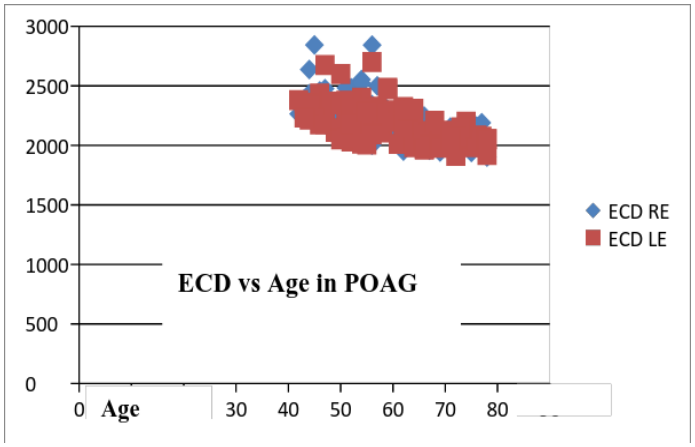

Table 1. Comparison of corneal endothelial cell changes among cases and control.

Left eye						Right eye				
P value	Control		Case		P value	Control		Case		Category
	SD	Mean	SD	Mean		SD	Mean	SD	Mean	
.000	101.31	2390.18	154.39	2198.20	.000	116.92	2417.43	171.49	2211.13	ECD
.000	2.89	48.71	6.85	43.58	.000	2.82	48.25	5.77	43.79	HX
.000	3.75	35.44	4.64	37.97	.000	3.80	34.56	4.82	38.13	CV

There was a significantly lower endothelial cell density and hexagonality among cases compared to controls. Coefficient of variation value was higher among cases compared to controls which are shown in Table 1.

Table 2. Association between severity of visual field defect and endothelial cell changes.

Left eye							Right eye							
P value	Advanced		Moderate		Early		P value	Advanced		Moderate		Early		Visual Field
	SD	Mean	SD	Mean	SD			SD	Mean	SD	Mean	SD	Mean	
.000	73.59	2016.67	129.50	2187.28	154.36	2269.99	.000	77.94	2025.42	116.78	2193.88	203.43	2297.94	ECD
.000	5.58	36.08	6.25	43.22	6.16	46.42	.000	4.72	38.08	5.21	42.96	5.04	46.89	HX
.000	3.69	42.83	4.36	38.40	3.94	35.87	.000	4.15	43.17	3.67	38.50	5.16	35.92	CV

As the severity visual field defect increased endothelial cell density and hexagonality decreased and coefficient of variation increased in our study.

Table 3. Endothelial cell changes in relation to duration of disease.

Left eye						Right eye						
CV		HX		ECD		CV		HX		ECD		Duration in years
SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	
3.96	34.75	6.40	47.58	149.10	2289.33	4.81	34.21	7.18	46.58	216.09	2337.33	< 5
4.23	37.89	5.84	43.78	144.06	2203.24	2.97	37.62	3.70	44.51	120.99	2213.62	5 - 9
4.10	39.53	7.08	41.09	142.10	2149.68	4.14	40.35	5.10	42.15	127.79	2151.21	10 - 14
4.72	43.40	6.22	39.80	111.53	2053.40	3.78	45.60	6.38	36.20	89.35	1994.40	≥ 15
.000		.002		.001		.000		.000		.000		P value

As the duration of disease increased, both ECD and HX decreased and CV increased in these patients.

Discussion

The corneal endothelium is a single layer of polygonal cells covering the posterior surface of Descemet's membrane. The endothelial cells have the lowest mitotic activity. The main function of the endothelium is regulation of hydration of cornea through ATP and biocarbonate-dependent pump and thereby providing transparency. In the adult, the average cell density is 2600 - 3000 cells/mm^2 and the percentage of hexagonal cells is about 60 - 75%. The central endothelial cell density decreases at an average rate of 0.6% per year. To maintain proper structure and function, endothelial cells respond to minor damage with stretching and centripetal migration into the injured area which lead to polymegathism and pleomorphism.[1] Normal values for pleomorphism and polymegathism are >59.0 and <30.0% respectively. It means that a normal healthy cornea should have at least 60% endothelial cells with regular shape or hexagonality and should not have abnormal endothelial cell sizes or areas (normal 312–320 micron square) in more than 30% of cells.[2] Endothelial cell density can be decreased as a result of trauma, refractive surgery, previous keratoplasty, diabetes, glaucoma, or endothelial dystrophies.[1] Glaucoma is a chronic optic neuropathy characterized by progressive loss of retinal ganglion cells, thinning of the neuroretinal rim and the retinal nerve fiber layer (RNFL), and with corresponding deterioration of the visual field. Early detection of glaucoma is essential for early treatment initiation and is therefore of great clinical importance in preserving vision.[3] It is one of the main cause of irreversible blindness worldwide, but typically remains asymptomatic until very severe. POAG is usually diagnosed during routine eye examination, which includes fundoscopic evaluation and visual field assessment (using perimetry).[4] As increased intraocular pressure causes structural and functional events, IOP should be controlled to prevent the loss of retinal ganglion cells.[5,6] Management of POAG mainly includes topical drug therapies and surgery to reduce IOP,

although new therapies targeting neuroprotection of RGCs and axonal regeneration are under development.[4] The ultimate goal of glaucoma management is the preservation of patients' visual function and quality of life (QoL).[7]

This study showed a significant decrease in endothelial density in patients with primary open angle glaucoma compared to age matched control group (p value- .000). Hexogonality and coefficient of variation also showed significant difference. According to Cho SW et al there was a significant decrease in corneal endothelial cell density in eyes with primary open-angle glaucoma, (2370.5 cell/mm^2, P < 0.001) than the normal group (2723.6 cell/mm^2). Elevated intraocular pressure likely affected the decrease of corneal endothelial cell density in eyes with glaucoma.[8] Gagnon et al also suggested that patients with glaucoma may have lower corneal endothelial cell density than those without glaucoma of the same age group. The mechanisms leading to lower endothelial cells in patients with glaucoma are not clear. The proposed mechanisms of endothelial cell damage are direct damage from increased IOP, congenital alteration of the corneal endothelium and trabecular meshwork in patients with glaucoma, glaucoma medication toxicity, or a combination of these factors.[9] Sihota R et al studied a significant decrease in the corneal endothelial cell density in eyes with acute angle closure glaucoma and in chronic PACG. The endothelial cell population in eyes with subacute PACG and in the fellow eyes of all subtypes of PACG was not significantly different from the normal population in this study.[10] Urban B et al observed a reduction of 13.0% in corneal endothelial cell density in primary open-angle glaucoma patients and 11.9% reduction in normal-tension glaucoma patients.[11] The study by Gatzioufas Z showed a decrease in mean endothelial density in primary congenital glaucoma.[12]Melamed et al observed morphologic changes in corneal endothelium in rabbits following rise in intraocular pressure, which are associated with decreased corneal endothelial density. He proved that high IOP may impact on the cornea in the following two ways. (1) elevated IOP influences the metabolic active-pumping mechanism, thus reducing resistance to aqueous flow to the stroma and consequent stromal edema, (2) high IOP causes morphological cellular damage, like cellular ruptures, swelling of mitochondria, disorganization of endoplasmic reticulum, and the existence of myelin bodies.[11] Various studies in pseudoexfoliation glaucoma also showed less endothelial cell counts. [2, 13] It was reported that the endothelial cell density was not correlated with the severity of glaucoma.[15] Wang M et al also reported that the endothelial cell density was not correlated with the severity of glaucoma in Chinese patients with pseudoexfoliation syndrome.[13] But in our study there was significant correlation with severity of visual field defects. As the severity of field defect increased ECD and hexogonality of corneal endothelial cells decreased. As Duration of disease prolonged ECD decreased which was also significant (p .000-.002).

Conclusion

In conclusion POAG can cause damage to the endothelium, these patients need to be evaluated with specular microscopy as majority of patients may need glaucoma or cataract surgery during treatment period. The ultimate goal is the preservation of patients' visual function and quality of life (QoL) by regular follow up and proper management.

References

1. Zavala J, López Jaime GR, Rodríguez Barrientos CA, Valdez-Garcia J. Corneal endothelium: developmental strategies for regeneration. Eye (Lond). 2013 May;27(5):579-88.
2. Wali UK, Al-Mujaini AS, Al-Kharusi NS, Bialasiewicz AA, Rizvi SG. Quantitative and qualitative corneal endothelial morphology of omani patients with pseudoexfoliation syndrome. Sultan

Qaboos Univ Med J. 2008Nov;8(3):300-5.
3. Kita Y, Soutome N, Horie D, Kita R, Holló G. Circumpapillary ganglion cell complex thickness to diagnose glaucoma: A pilot study. Indian J Ophthalmol. 2017 Jan;65(1):41-47.
4. Weinreb RN, Leung CK, Crowston JG, Medeiros FA, Friedman DS, Wiggs JL, Martin KR. Primary open-angle glaucoma. Nat Rev Dis Primers. 2016 Sep 22;2:16067.
5. Iutaka NA, Grochowski RA, Kasahara N. Correlation between Visual Field Index and Other Functional and Structural Measures in Glaucoma Patients and Suspects. J Ophthalmic Vis Res. 2017 Jan-Mar;12(1):53-57.
6. Harwerth RS, Wheat JL, Fredette MJ, Anderson DR. Linking structure and function in glaucoma. Prog Retin Eye Res. 2010;29:249–271.
7. Quaranta L, Riva I, Gerardi C, Oddone F, Floriano I, Konstas AG. Quality of Life in Glaucoma: A Review of the Literature. Adv Ther. 2016 Jun;33(6):959-81.
8. Cho SW, Kim JM, Choi CY, Park KH. Changes in corneal endothelial cell density in patients with normal-tension glaucoma. Jpn J Ophthalmol. 2009Nov;53(6):569-73.
9. Gagnon MM, Boisjoly HM, Brunette I, Charest M, Amyot M. Corneal endothelial cell density in glaucoma. Cornea. 1997 May;16(3):314-8.
10. Sihota R, Lakshmaiah NC, Titiyal JS, Dada T, Agarwal HC. Corneal endothelial status in the subtypes of primary angle closure glaucoma. Clin Exp Ophthalmol.2003 Dec;31(6):492-5.
11. Urban B, Bakunowicz-Łazarczyk A, Michalczuk M, Krętowska M. Evaluation of corneal endothelium in adolescents with juvenile glaucoma. J Ophthalmol. 2015;2015:895428.
12. Gatzioufas Z, Labiris G, Stachs O, Hovakimyan M, Schnaidt A, Viestenz A, Käsmann-Kellner B, Seitz B. Biomechanical profile of the cornea in primary congenital glaucoma. Acta Ophthalmol. 2013 Feb;91(1):e29-34.
13. Wang M, Sun W, Ying L, Dong XG. Corneal endothelial cell density and morphology in Chinese patients with pseudoexfoliation syndrome. Int J Ophthalmol. 2012;5(2):186-9.
14. Bozkurt B, Güzel H, Kamış Ü, Gedik Ş, Okudan S. Characteristics of theAnterior Segment Biometry and Corneal Endothelium in Eyes with Pseudoexfoliation Syndrome and Senile Cataract. Turk J Ophthalmol. 2015 Oct;45(5):188-192.
15. Vannas A, Setälä K, Ruusuvaara P. Endothelial cells in capsular glaucoma. Acta Ophthalmol (Copenh). 1977 Dec;55(6):951-8.