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A STUDY OF THE DETERMINATION OF CORNEAL ENDOTHELIAL CELL COUNT IN PATIENTS WITH PRIMARY GLAUCOMA

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ABSTRACT

Introduction: Present study aimed to determine the corneal endothelial cell count in adult patients with primary glaucoma (POAG, PACG and NTG) and to compare the corneal endothelial cell count in age matched normal individuals.

Materials & Methods: The study was conducted at the Ophthalmology Department of Bharati Hospital, Pune. A total of 194 eyes of patients having primary glaucomas (POAG, PACG, NTG) between age group of 20 to 80 were included in this study along with 196 eyes of age matched controls (with no ocular complaints or systemic ailments). The endothelial cell count in both the groups was measured with the help of specular microscope. Data was analysed by SPSS ver. 21.0.

Results: The average endothelial cell count in the POAG was 2661.342 cells/mm2 and in PACG was 2280.22 cells/mm2 and in NTG was 2614.67 cells/mm2 and in the control group was 2781.21 cells/mm2. There was significant ($p<0.05$) endothelial cell loss in POAG and PACG in age groups of 40 to 80 years of age but the cell loss was not significant in NTG group in 40 to 60 age group ($p<0.05$). There was no significant cell loss in age group of 20 to 40 years in all glaucoma types.

Conclusion: Endothelial cell counts were significantly lower in patients with POAG and PACG when compared with controls. Thus evaluation of corneal endothelium is necessary before proceeding to intraocular procedures in glaucoma patients.

KEYWORDS : Endothelial cell count, Normal tension glaucoma, Primary angle closure glaucoma, Primary open angle glaucoma

INTRODUCTION

The cornea is the anterior most structure of the eye which is transparent and avascular. Histologically it consists of 6 layers namely Epithelium, Bowman layer, Stroma, Dua's layer, Descemet membrane and Endothelium.[1]The refractive power of cornea is about +43D which is three fourth of the total refractive power of the eye (60D).[1] The average horizontal diameter of the cornea is 11.75 mm and vertical diameter 11.5mm.[2]The shape of the cornea is prolate, being steeper centrally as compared to the periphery.[1]

The endothelium consists of a single layer of hexagonal cells which plays an important role in maintaining the transparency of the cornea [1]. These cells do not have the ability to regenerate.[1]The normal density of corneal endothelial cells at birth is around 6000 cells/ mm^2 which is reduced to about 2400-3000 cells/ mm^2 in adults.[1] The endothelial cell count decreases by approximately 0.5%-0.6% (100–200 cells) per year.[3]The defect left by the dying cells is filled by enlargement (polymegathism) of the remaining cells which leads to increase in corneal thickness. Therefore, corneal decompensation occurs when the count becomes less than 500 cells/mm^2 that leads to corneal oedema and loss of transparency. Corneal hydration is maintained at a constant level by a fluid pump mechanism (Na+—K+ ATPase) that is located predominantly on the corneal endothelium but is also present at the corneal epithelium.[1] It has been proved that human corneal endothelial cells have mitotic ability in vitro but in vivo they are arrested in G1 phase.[4]

The health of the corneal endothelium is best detected by specular microscope. Mild endothelial stress may result in cell size and shape changes, while greater stress results in cell loss as well as irreversible changes to the endothelium. Stress factors may be metabolic (from hypoxia or hyperglycaemia), toxic (from drugs or their preservatives), injury (from trauma or surgery), or alterations in pH or osmolarity.[5]

A broad range of disorders can affect the endothelium, such as glaucoma, dry eye, and diabetes mellitus. One of the common conditions that affects the corneal endothelium is Glaucoma.

Glaucoma has a worldwide prevalence of 3.5% in the population aged 40-80 years, with many of these patients undergoing varied levels of medical and surgical treatments to prevent progression of glaucoma, often with unintended and unknown consequences on the corneal endothelium.[6] Many factors affect the corneal endothelium in the patients of glaucoma including direct damage due to elevated pressure (IOP), congenital changes, ocular surgery, and ocular trauma.[7]

Reduced cell densities have been reported in association with open angle glaucoma and angle closure glaucoma than in normal tension glaucoma when compared with age matched individuals.[8,9]

In this study, we compared the changes in corneal endothelial cell density between primary open angle glaucoma, closed angle glaucoma and normal tension glaucoma.

MATERIALS AND METHODS

Present study was conducted at the Ophthalmology Department of Bharati Hospital, Pune. A total of 100 patients (n - 194) having primary glaucoma between age group of 20 to 80 attending the glaucoma OPD were enrolled in this study. Similarly a total of 100 (n - 196) age matched controls with no ocular complaints or systemic ailments were enrolled as the control group. Prior consent from the patients and ethical committee clearance was obtained.

Cases with viral infections (like herpes zoster, herpes simplex, cytomegalovirus), any kind of intraocular surgery (like cataract surgery, glaucoma surgery like trabeculectomy, trabeculotomy, peripheral iridectomy etc.), ocular trauma, conditions affecting cornea (like Fuchs's dystrophy, Keratoconus, Aphakic bullous keratopathy, Pseudophakic bullous keratopathy, Pseudo-exfoliation) and Systemic causes (like diabetes mellitus) were excluded.

General patient information was noted from every subject like age, sex and presenting complaint. The ophthalmological examination included:

1. Best corrected visual acuity on Snellen's chart
2. Detailed slit lamp evaluation on the Topcon SL-D301
3. Fundus examination by Volks 90 D lens after complete mydriasis
4. Intraocular pressure by applanation tonometry
5. Gonioscopy
6. Specular microscopy of Topcon SP-1P-This is a non-invasive procedure wherein the patient sits on a chair and places his chin on the chin rest of the machine while the machine evaluates and examines the cornea and displays information regarding the same on the screen of the machine.

All the data was noted down in a pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables will be assessed by Chi-Square test. Quantitative data was represented using Mean ± SD. Analysis of Quantitative data between the two groups was done using unpaired t-test if data passed 'Normality test' and by Mann-Whitney Test if data failed 'Normality test'. A p-value < 0.05 was taken as level of significance. Results were graphically represented where deemed necessary. SPSS Version 21 was used for analysis.

RESULTS

Out of 194 eyes of patients diagnosed with primary: 114 eyes were of primary open angle glaucoma (POAG), 46 eyes were of primary angle closure glaucoma (PACG) and 34 eyes were of normal tension glaucoma (NTG). Average endothelial cell count was significantly lower among cases of Glaucoma as compared to controls, in age group of 40-80 years while the counts were lower but not significant in age group of 20-40 years of age (p-0.14) (Table 1). On comparison of endothelial cell count among POAG, PACG and controls, we observed similar results with significantly lower count in age range of 40-60 years (p<0.05) (Table 2 & 3). In these groups, no difference was observed with regard to endothelial count between cases and controls in the age group of 20-40 years (Table 2 & 3). However, in NTG cases, the difference was observed only in age group of 60-80 years of age (Table 4).

DISCUSSION

Corneal endothelial cells play an important role in maintaining corneal transparency by keeping the cornea in a dehydrated state. Once the cells are damaged they do not regenerate but instead enlarge in size.[10] The main function of the endothelium is regulation of hydration of cornea through ATP and bicarbonate 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.[11]

The mechanisms leading to lower endothelial cell counts in patients with glaucoma are not clearly defined, but Gagnon et al. [7] formulated three hypothesis a) direct damage from increased IOP, b) congenital alteration of the corneal endothelium and trabecular meshwork in patients with glaucoma, c) glaucoma medication toxicity, or a combination of these factors. Thus, corneal endothelial cell density is often reduced in the eyes of glaucoma patients.[12] Reduced endothelial cell densities are reported in open-angle glaucoma different subtypes of angle-closure glaucoma and normal tension glaucoma. Knorr et al. reported a 31% reduction in corneal endothelial cell density in primary open-angle glaucoma (POAG) patients compared with a normal control group.[13] Cho et al reported 13% reduction in POAG group[8], Similar results were observed in the study done by Gagnon et al where in 13% reduction was noted in POAG group and 11.9% reduction in NTG group.[7]

The present case control study aimed at determining the corneal endothelial cell count in patients with primary glaucoma (primary open angle, primary angle closure glaucoma, normal tension glaucoma) and in normal adults and to compare the endothelial cell count in both the groups. A total of 194 eyes of patients with primary glaucoma (114 POAG, 46 PACG and 34 NTG) and 196 eyes of age matched controls were included in our study.

Of the patient studied, 57% had POAG, 23% had PACG and 17% had NTG. In various studies the incidence of POAG has been 27%, 29%, 37%, and 41% as conducted by Das J et al. [14] Jacob A et al. [15] and Dandona L et al. [16] respectively. The ratio of POAG to PACG in our study was 7.7:1 similar to study done by Raychaudhuri et al where in his study the ratio was 10.1.[17] Congdon reported that in Caucasian races, Primary Open Angle Glaucoma accounted for 75-95% of the primary glaucoma's, with the disease presenting later in life and with less severe presentation.[18] Quigley in his study also found that Primary Open Angle Glaucoma was the most common form of glaucoma in many countries and accounted for 60-70% of the cases in the United States.[19]

In Asia, population-based studies from China and India have reported that significant percentage of population suffers from angle closure glaucoma than primary open angle glaucoma with an incidence of 10.3 %.[20] Scharioth noted that closed-angle glaucoma accounted for less than 14% of glaucoma cases in the United States and Europe, but as much as half of the glaucoma cases in other nations (particularly Asian countries).[21] However, in our analysis PACG formed only 23% of the eyes.

The endothelial cell count (cells/mm^2) maximum, minimum and average in all 3 groups of glaucoma was lower when compared with age matched controls. When we individually compared the endothelial cell count in POAG, PACG and NTG between 20 to 40 age group, it was seen that there was no significant (P>0.05) endothelial cell loss noted which can be explained by the probable recent onset of glaucoma. We found significant (P<0.05) low endothelial cell count in age groups of 40-80 in POAG, PACG, NTG when compared with controls. Korey M et al. [22] also studied central endothelial cell density and central corneal thickness in ocular hypertensives and primary open angle glaucoma and observed that there was decrease in central corneal endothelial cell density (P =0.001) with increasing age. Similar study done by Prasanna kumary C et al. [23] also showed a significant decrease in endothelial density in patients with primary open-angle glaucoma compared to age-matched control group (p<0.001). The mean endothelial cell density (ECD) in POAG patients were significantly lower (2211.13 ±171.49 cells/mm in right eye, 2198.20± 154.39 cells/mm in left eye) compared to control group (2417.43 ± 116.92 in right eye and 2390.18 ±101.31 cells/mm in left eye). Cho SW et al. [8] found a significant decrease (p< 0.001) in corneal endothelial cell density in eyes with primary open-angle glaucoma (2370.5 cell/mm^2) and no significant decrease P =1.000 in NTG, (2696.7 cells/mm^2) when compared with the normal group (2723.6 cell/mm^2).

In our study endothelial cell count in POAG group was 2661.3 cells/mm^2, NTG was 2614.76 cells/mm^2 and in controls was 2781.2 cells/mm^2 there was no significance noted among patients 40-60 age group in NTG subtype similar to results of the above studies. There was significant endothelial cell loss in patients among 60 to 80 age group which can be explained by increasing age. Significant endothelial cell loss was noted in patients of POAG group (p<0.05). Gagnon et al. [7] also suggested that patients with glaucoma may have lower corneal endothelial cell density (2154 ±419 cells/mm^2) than those without glaucoma (2560±306 cells/mm^2) of the same age group. Sihota R et al. [25] studied the corneal endothelial cell density in eyes with acute angle-closure glaucoma and in chronic PACG where they found that there was significant decrease in the corneal endothelial cell density in eyes that have had an acute attack of angle closure glaucoma and in eyes with chronic PACG. PACG in our study had significant endothelial cell loss (2280.22 cells/mm^2) when compared with controls (2781.2 cells/mm^2) (p<0.05). A further study by Nishant Sultana et al. [24] in patients of primary angle closure glaucoma stated that the endothelial cell density was 2104 cells /mm^2 in eyes with acute attack and 2615 cells/mm^2 in the other eye. The endothelial cell count was 1861 cells/mm^2 when the attack lasted for more than 72 hours and 2254 cells/mm^2 when the attack lasted for less than 72 hours. He also observed a significant reduction of corneal endothelial cell count by 20% following an acute attack of angle closure glaucoma. But we did not observe endothelial count at different time periods. Bigar F et al. [26] found a decrease in the endothelial count by 33% when compared to fellow eyes of acute angle closure glaucoma. The mean endothelial cell density in the affected eye was 1534 and in the unaffected fellow eye 2243 cells/mm^2 in their study. They concluded that a decrease in number of endothelial cells after acute angle-closure glaucoma frequently combined with cornea guttata accounted for the corneal degeneration in these patients following cataract extraction. A similar study done by Malaise-Stals J et al. [27] in patients of acute angle closure glaucoma when compared to control eyes found a significantly decreased endothelial count. The mean endothelial cell density in acute angle closure glaucoma was 1640 cells/mm^2 and in control group was 2398 cells/mm^2 (p-value<0.01).

CONCLUSION

Endothelial cell counts were significantly lower in patients with POAG and PACG when compared with controls. The proposed mechanisms are direct damage from IOP, congenital alteration of the corneal endothelium in patients with glaucoma, glaucoma medication toxicity, or a combination of these. Thus evaluation of corneal endothelium is necessary before proceeding to intraocular procedures in glaucoma patients.

Table 1. Age distribution of average endothelial cell count (cells/mm^2) in glaucoma cases versus controls

Age in Years	Glaucoma	Controls	p-value
20-40	2762.3±300	2924.75±222	**0.142**
40-60	2570.9±307	2794.3±259	**<0.001**
60-80	2485.1±322	2783.4±195	**<0.001**

Table 2. Age distribution of average endothelial cell count (cells/mm^2) in POAG cases versus controls

Age in Years	POAG	Controls	p-value
20-40	2887.5±302	2924.75±219	**0.38**
40-60	2603.97±309	2794.39±260	**<0.001**
60-80	2596.06±318	2783.29±201	**<0.001**

Table 3. Age distribution of average endothelial cell count (cells/mm^2) in PACG cases versus controls

Age in Years	PACG	Controls	p-value
20-40	2282.5±311	2924.75±226	**0.99**
40-60	2326.8±303	2794.39±249	**<0.001**
60-80	2142.4±321	2780.29±188	**<0.001**

Table 4. Age distribution of average endothelial cell count (cells/mm^2) in NTG cases versus controls

Age in Years	NTG	Controls	p-value
20-40	2877.2±319	2924.7±221	**0.114**
40-60	2699.4±309	2798.7±243	**0.064**
60-80	2691.3±327	2783.3±192	**0.003**

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