A cross sectional study on evaluating the corneal endothelial cell density and central corneal thickness in eyes with primary glaucoma

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ABSTRACT

Background: This study aims at evaluating glaucoma-induced damage to the corneal endothelium and the effect of central corneal thickness (CCT) on the intra-ocular pressure (IOP) measurement in patients newly diagnosed with primary glaucoma. Methods: It is a hospital-based cross-sectional study involving 60 newly diagnosed primary glaucoma patients >18 years. They underwent fundus examination, four-mirror gonioscopy, and perimetry for confirming the diagnosis. Evaluation and analysis of corneal endothelial cell density and CCT were performed. Chi square test was performed to find out the association between glaucoma, corneal endothelial cell density, and CCT. Results: Evaluation of 60 patients revealed that by age distribution, the corneal endothelial cell density was lower in the 51–65 year age group and an age-related decrease in corneal endothelial cell density and CCT was found in newly diagnosed primary glaucoma patients. The mean CCT was 525 micrometers in patients with IOP between 20 to 40 mm Hg and 528 micrometers in patients with IOP between 41 to 60 mm Hg. The mean corneal endothelial cell density was 2361 cells/mm² in primary open-angle glaucoma (POAG) and 2284 cells/mm² in primary angle-closure glaucoma (PACG). The mean CCT was 525 micrometers in POAG and 528 micrometers in PACG. Conclusions: The corneal endothelial cell density was lower in patients with PACG when compared with POAG, and the average CCT showed no significant difference in POAG and PACG patients. However, CCT was increased in patients with a higher intra-ocular pressure. The corneal endothelial cell density was lower in patients with a high intra-ocular pressure.

Keywords: CCT (central corneal thickness), IOP (intra-ocular pressure), PACG (primary angle-closure glaucoma), POAG (primary open-angle glaucoma)

Introduction

Glaucoma is a group of disorders characterized by progressive optic neuropathy, resulting in a characteristic appearance of an optic disc (structural change) and a specific pattern of irreversible visual field defects that are associated frequently but not invariably with raised intra-ocular pressure (IOP). Glaucomas are primarily classified as developmental, primary acquired, and secondary glaucomas. Primary Glaucomas may be further classified as primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG included). The corneal endothelium is a single layer of hexagonal-shaped cells which plays a vital role in maintaining the clarity of vision. The corneal endothelium is important in maintaining a healthy and clear cornea. Its primary function is to regulate the hydration of the cornea through active...
ion transport, and alterations in this hydration pre-dispose to corneal swelling and loss of clarity as endothelial cells have limited regenerative capacity.\textsuperscript{[3]} Glaucoma has a worldwide prevalence of 3.5% of 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.\textsuperscript{[4]} Glaucoma is associated with deleterious effects on the corneal endothelium. Damage to the corneal endothelium may be caused by the disease process itself as well as by its treatment. The mechanism involved in glaucoma-associated damage to the corneal endothelium is important for protecting corneal clarity and visual acuity in all glaucoma patients. Many factors affect the corneal endothelium in glaucoma patients, including direct damage because of elevated intra-ocular pressure, congenital changes, ocular surgery, and ocular trauma;\textsuperscript{[5]} thus, the corneal endothelial cell density is often reduced in the eyes of glaucoma patients. Reduced cell densities have been reported in association with open-angle glaucoma and angle-closure glaucoma. Knorr et al\textsuperscript{[6]} reported a 31% reduction in the corneal endothelial cell density in POAG patients compared with a normal control group. Sihota et al\textsuperscript{[7]} reported a significant decrease in the corneal endothelial cell density in eyes with angle-closure glaucoma.

Many studies have reported changes in the corneal endothelial cell density in both open-angle glaucoma and angle-closure glaucoma. \textsuperscript{[8,9]} IOP is an important parameter in the diagnosis and management of glaucoma. Although Goldmann applanation tonometry is the preferred method for the measurement of IOP, several factors, including central corneal thickness, may influence its accuracy.\textsuperscript{[10]} Patients with thinner corneas tend to have under-estimated IOP, whereas those with thicker corneas tend to have over-estimated IOP.\textsuperscript{[11]} If a patient has an abnormal central corneal thickness (CCT), the true IOP level may be masked, resulting in under-treatment or over-treatment of glaucoma.

**Objective**

To evaluate the corneal endothelial cell density and CCT in newly diagnosed primary glaucoma patients attending a tertiary care hospital.

**Materials and Methods**

This was a hospital-based cross-sectional study conducted in the department of ophthalmology in a medical college hospital. The approval from Institutional Ethics Committee was obtained on 20/08/2018.

This study included 60 newly diagnosed primary glaucoma patients of >18 years of age. The data were collected from the newly diagnosed primary glaucoma patients for 1 year from September 2018 to August 2019.

**Inclusion criteria**

Newly diagnosed patients with primary glaucoma of >18 years of age with a rise in IOP >21 mmHg on more than one occasion are classified by the following findings:

**Primary open-angle glaucoma**

- IOP >21 mmHg with clinical glaucomatous optic nerve damage.
- An open anterior chamber angle by gonioscopy.
- Characteristic visual field loss in perimetry.
- The absence of signs of secondary glaucoma or a non-glaucomatous cause for the optic neuropathy.

**Primary angle-closure glaucoma**

- IOP >21 mmHg with clinical glaucomatous optic nerve damage.
- Gonioscopy showed posterior trabecular meshwork and iridotrabecular contact in three or more quadrants.
- Characteristic visual field loss in perimetry.
- The absence of signs of secondary glaucoma or a non-glaucomatous cause for the optic neuropathy.

**Exclusion criteria**

Patients with H/O corneal disease, contact lens wear, ocular surgery, and ocular trauma were excluded from the study.

After obtaining approval from the Institutional Ethics Committee, 60 patients meeting the criteria of our study were given a brief introduction regarding the purpose of our study after getting the written informed consent in English and in the regional language. Visual acuity, anterior segment, anterior chamber depth, pupil, lens, Goldmann’s applanation tonometry, indentation gonioscopy (modified Schaffer’s grading), and fundus examinations were performed in patients who had IOP greater than 21 mmHg on more than one occasion to achieve the clinical diagnosis of primary glaucoma. Gonioscopy was performed with a Zeiss four-mirror goniolens. Visual field evaluation was performed using a Zeiss automated Humphrey visual field analyzer 750i to establish the diagnosis. In newly diagnosed patients with primary glaucoma, corneal endothelial cell density was evaluated by specular microscopy and CCT was evaluated by pachymetry. A TOPCON SP 3000P model machine was used for both specular microscopy and pachymetry.

**Data compilation and analysis**

Data entry and analysis were performed using SPSS 16.0 for Windows software. Percentage and P values were collected. 95% confidence interval was also estimated. Chi square test was performed to find out the association between glaucoma, corneal endothelial cell density, and CCT.

**Results**

**Age distribution**

Among the 60 patients, 22 patients were in the age group of 35–50 years and 38 patients were in the age group of 51–65 years. The mean corneal endothelial cell density was 2358 cells/mm² in the 35–50 year age group. The mean corneal endothelial
cell density was 2332 cells/mm² in 51–65 years. The corneal endothelial cell density was lower in the 51–65 year age group when compared to the 35–50 year age group. There was an age-related decrease in the corneal endothelial cell density in newly diagnosed primary glaucoma patients. The mean CCT was 529 micrometers in the 35–50 year age group and 522 micrometers in the 51–65 year age group. There was an age-related decrease in CCT in newly diagnosed primary glaucoma patients in our study. Details are in Figures 1 and 2.

**Sex distribution**

Among the 60 patients, 24 were males and 36 were females. The mean corneal endothelial cell density was 2357 cells/mm² in males and 2348 cells/mm² in females. The mean corneal endothelial cell density was lower in females compared to males. The mean CCT was 523 micrometers in males and 526 micrometers in females. Details are shown in Figures 3 and 4.

**Distribution with intra-ocular pressure**

Among the 60 patients, 44 patients had IOP between 20 to 40 mm Hg and 16 patients had IOP between 41 to 60 mm Hg. The mean corneal endothelial cell density was 2361 cells/mm² in patients with IOP between 20 and 40 mm Hg and 2284 cells/mm² with IOP between 41 and 60 mm Hg. Eyes with a high IOP range showed a lower average corneal endothelial cell density. The mean CCT is 525 micrometers in patients with IOP between 20 and 40 mm Hg and 528 micrometers in patients with IOP between 41 and 60 mm Hg. The CCT was higher in patients with high IOP. Details are shown in Tables 1 and 2.

**Distribution with glaucoma**

Among the 60 patients, 44 patients had POAG and 16 patients had PACG. The corneal endothelial cell density was lower in patients with PACG when compared with POAG. The average corneal endothelial cell density and CCT in POAG patients were 2361 cells/mm² and 525 microns, respectively. The average corneal endothelial cell density and CCT in PACG patients were 2284 cells/mm² and 528 microns, respectively. Details are shown in Figures 5 and 6.

**Discussion**

Sixty patients were included in this study based on the inclusion and exclusion criteria to evaluate the corneal endothelial cell density and CCT in newly diagnosed primary glaucoma patients. By age distribution, the corneal endothelial cell density was lower in the 51–65 year age group when compared to the 35–50 year age group. There was an age-related decrease in the corneal endothelial cell density, and there was an age-related decrease in CCT in newly diagnosed primary glaucoma patients in our study. Other studies performed by Rao SK et al.,[10] Yunliang S et al.,[11] Yee RW et al.,[12] and Bourne WM et al.[13] had shown an endothelial cell loss with aging, and it ranges between 0.3 and 0.6% per year. In another study, the mean CCT was 519.57 micrometers in males and 522.37 micrometers in females.[14] Other studies have shown that CCT in females was found to be higher than that in males,[15] lower than that in males,[16] and independent of gender.[17]

In our study, the corneal endothelial cell density was lower in patients with high IOP. The mean CCT was 525 micrometers in patients with IOP between 20 and 40 mm Hg and 528 micrometers in patients with IOP between 41 and 60 mm Hg. In our study,
the CCT was higher in patients with high IOP. Increased IOP has been said to have no effect on CCT,\textsuperscript{[18]} to increase it,\textsuperscript{[19]} and to decrease it.\textsuperscript{[20‑22]}

The mean corneal endothelial cell density was 2361 cells/mm\textsuperscript{2} in POAG and 2284 cells/mm\textsuperscript{2} in PACG. The corneal endothelial cell density was lower in patients with PACG when compared with patients with POAG in our study. In another study, the mean corneal endothelial cell density was 2079 ± 270.6 cells/mm\textsuperscript{2} in POAG.\textsuperscript{[23]} Sihota measured the corneal endothelial cell density in sub-types of PACG, and the mean corneal endothelial cell density was 1597 ± 653 cells/mm\textsuperscript{2} in acute PACG, 2396 ± 271 cells/mm\textsuperscript{2} in sub-acute PACG, and 2229 ± 655 cells/mm\textsuperscript{2} in chronic PACG.\textsuperscript{[5]} Corneal endothelial cell loss has been well documented in eyes presenting with an acute attack of angle-closure glaucoma.\textsuperscript{[24‑26]}

In our study, the mean CCT was 525 micrometers in POAG and 528 micrometers in PACG. In another study, the average CCT in POAG was 518.69 micrometers.\textsuperscript{[14]} Sihota measured the CCT in sub-types of PACG, and the mean CCT was 567.9 micrometers in acute PACG, 531.4 micrometers in sub-acute PACG, and 526.4 micrometers in chronic PACG.\textsuperscript{[23]}

**Conclusion**

Our study on evaluation of corneal endothelial cell density and CCT in primary glaucoma patients concluded that the corneal endothelial cell density is lower in patients with PACG when compared with patients with POAG and the average CCT showed no significant difference in POAG and PACG patients, but the CCT is increased in patients with higher IOP. This necessitates complete evaluation of glaucomatous eyes (especially PACG > POAG) inclusive of corneal parameters such as thickness and endothelial cell density at the time of diagnosis as well as follow-up for planning appropriate management. The limitation of this study is that because of a smaller sample size, it is difficult to extrapolate the result to the general population.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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