CORNEAL ENDOTHELIAL CELL DENSITY IN ACUTE ANGLE CLOSURE GLAUCOMA

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ABSTRACT

BACKGROUND

Angle closure is characterised by apposition of the peripheral iris against the trabecular meshwork resulting in obstruction of aqueous outflow. Acute angle-closure glaucoma is characterised by pain, redness and blurred vision. The pain is typically a severe deep ache that follows the trigeminal distribution and maybe associated with nausea, vomiting, bradycardia and profuse sweating. The blurred vision, which is typically marked maybe caused by stretching of the corneal lamellae initially and later oedema of the cornea as well as a direct effect of the IOP on the optic nerve head. The modifications in corneal endothelial cell density after a crisis of angle-closure glaucoma is being evaluated.

AIMS AND OBJECTIVES

The objective of the study is to assess the corneal endothelial cell count (density) by specular microscopy in patients presenting with acute angle-closure glaucoma.

METHODS

Corneal endothelial cell counts of 20 eyes of patients with PACG with an earlier documented symptomatic acute attack unilaterally were compared with 20 fellow eyes. Evaluation of patient included visual acuity, intraocular pressure, gonioscopy, disc findings and specular microscopy.

RESULTS

The mean endothelial cell density was 2104 cells/mm^2 in the eye with acute attack and 2615 cells/mm^2 in the fellow eye. The average endothelial cell count when the duration of attack lasted more than 72 hours was 1861 cells/mm^2.

CONCLUSION

Corneal endothelial cell density was found to be significantly reduced in eyes following an acute attack of primary angle closure glaucoma.

KEYWORDS

PACG - Primary Angle Closure Glaucoma, Corneal Endothelial Cell Count, Specular Microscopy.

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INTRODUCTION: Glaucoma is ranked as the leading cause of irreversible blindness worldwide by the World Health Organization. It was estimated that by 2010, 3.9 million people with glaucoma would be blind due to Primary Angle Closure Glaucoma (PACG). By 2020, this number is projected to increase to 5.3 million.[1] Eighty-six percent of people with PACG are in Asia with approximately 48.0% in China, 23.9% in India and 14.1% in Southeast Asia.[2] These staggering statistics highlight the necessity to elucidate risk factors relevant to angle closure determining clinical markers for progression of disease distinguishing differential responses and complications of interventions and discovering clues as to underlying pathogenic mechanisms.

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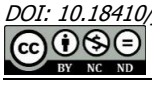


Management of patients with PAC depends on the type of clinical presentation making the diagnosis of PACS, PAC or PACG as well as correctly identifying the underlying pathophysiology and for the individual patient this scheme of the natural history of primary angle closure addresses both the prognosis for progression and the stage-appropriate need for treatment.[2] Primary acute angle closure glaucoma is a subtype of Primary Angle Closure Glaucoma (PACG) with an acutely elevated Intraocular Pressure (IOP). According to the World Health Organization, the patient presenting with acute angle closure glaucoma, the IOP is estimated to rise more than 60 mmHg and is associated with a profound reduction in central visual acuity.

Characteristic findings include conjunctival hyperaemia, a cloudy cornea, and an irregular (usually vertically oval), mid-dilated, fixed pupil. The diagnosis of pupillary block glaucoma has several facets. During the course of every ocular examination, the physician must consider general risk factors in the medical history and look for anatomic features that may predispose to angle closure. The gold standard examination is gonioscopy, which is essential in identifying

eyes with some form of angle closure or those at increased risk for angle-closure glaucoma (i.e., Occludable angles). In other situations, the patient may present with signs and symptoms suggesting angle-closure glaucoma and the correct diagnosis will depend on an understanding of the symptoms, predisposing circumstances, physical findings of the disease and the differential diagnosis.

Corneal endothelial cell density is reported to be decreased following acute attacks of angle closure glaucoma.[3] Histological studies have shown that acute intraocular hypertension alters corneal endothelial status. Using specular microscopy, endothelial cell count can be estimated. Corneal endothelial cells are found to play an important role in maintaining the corneal clarity. They maintain the dehydrated state of the corneal stroma and allow the orderly lattice of collagen fibrils to create a transparent tissue.[4]

AIM AND OBJECTIVES: The aim of the study was to assess the corneal status in eyes presenting with acute angle closure attack. Acute angle closure glaucoma is characterised by an acute rise in intraocular pressure in the range of 50-60 mmHg. The signs are intense ciliary congestion and a hazy cornea. The corneal haze is due to the epithelial and stromal oedema, which is observed using slit lamp biomicroscopy. This influences the morphology and physiology of the corneal endothelial cells by altering the endothelial pump mechanism. In this process, the corneal endothelial cells are lost and damaged. However, quantification of this entity can be done using specular microscopy and the exact cellular loss and morphology can be studied. The objective of the study is to assess the corneal endothelial cell count (density) by specular microscopy in patients presenting with acute angle-closure glaucoma and before any interventional treatment in order to assess possible damage during pressure induced abnormal hydration of the cornea.

MATERIALS AND METHODOLOGY: Study was conducted between July 2015 and February 2016. 20 patients (8 males, 12 females) were enrolled with an average age of 52 years and an earlier documented symptomatic acute attack were studied and compared to fellow eye without an history of acute attack. Patients with eye disease, which can affect corneal endothelium status (Uveitis, Trauma, Ocular Surgery, Keratitis, Pseudoexfoliative glaucoma, Open angle glaucoma) were excluded from study. The duration of attack ranged from 1 day to 15 days. The increase in IOP ranged from 34-74 mmHg.

Detailed evaluation including visual acuity, IOP using Goldmann applanation tonometer, gonioscopy using Goldmann single mirror lens, disc evaluation wherever possible and specular microscopy being a noncontact method was done to determine the corneal endothelial cell count using dot method and results documented. A detailed specular microscopy study for corneal endothelial cell count and morphology was studied.

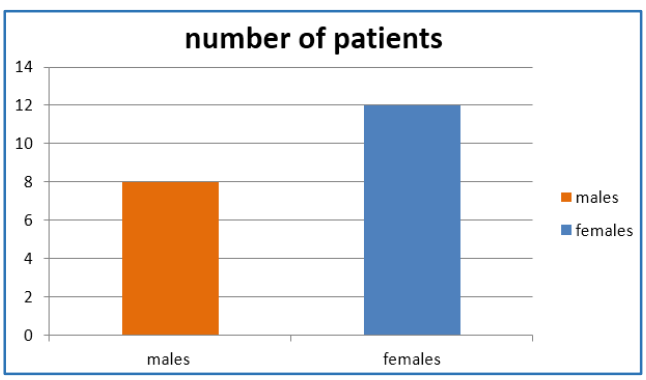
Inclusion Criteria:

1. Eyes with primary acute angle closure glaucoma.
2. Males and females in the age group between 40-60 years.

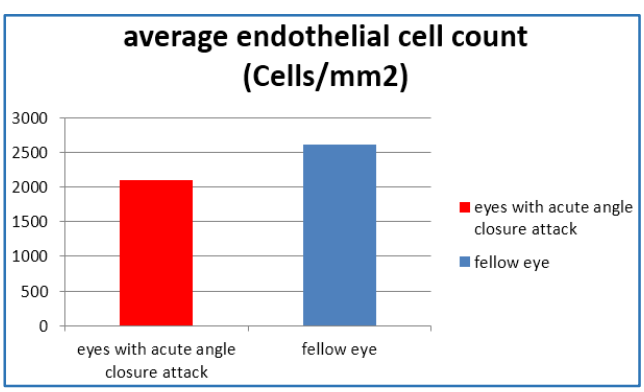
Exclusion Criteria: Patients with eye diseases that can affect corneal endothelial status were excluded from study.

- Pseudoexfoliative Glaucoma.
- Open Angle Glaucoma.
- Uveitis.
- Trauma.
- Previous Ocular Surgery.
- Keratitis.

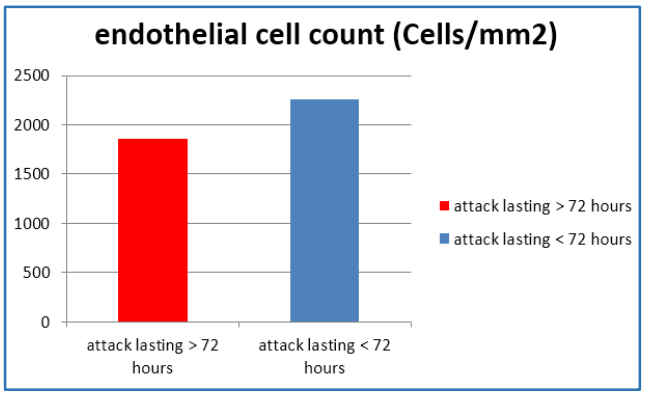
RESULTS: Of the 20 patients enrolled in the study, 8 were males and 12 females.



In our study, the average raise in IOP in eyes with an acute attack was 54 mmHg. The mean endothelial cell count in eyes with an acute attack of PACG was 2104 cells/mm^2 and 2615 cells/mm^2 in the fellow eyes. There is a 20% reduction in the mean endothelial cell density as compared to the fellow eye.



The duration of attack had a significant impact on the endothelial count. The mean endothelial count was 1861 cells/mm^2 when attack lasted more than 72 hours and 2254 cells/mm^2 when the attack lasted less than 72 hours.



DISCUSSION: Angle closure is characterised by apposition of the peripheral iris against the trabecular meshwork resulting in obstruction of aqueous outflow. The term glaucoma is used if there is evidence of glaucomatous optic nerve damage.[5] The end condition of primary angle closure glaucoma includes the fundamental criteria for any glaucoma: damage to the optic nerve with concomitant loss of visual field function. Hence, the screening strategies for epidemiologically detecting this advanced stage of PACG becomes very important. Considering the implications of the high rates of PACG found in surveys of select Chinese and Indian populations affecting nearly 2% of individuals over the age of 40 years old: with nearly half of the world's population living in India and China, scores of millions of people potentially require iridotomy.

For deciding the management and followup options, the clinician too must determine whether the presenting eye is a PAC suspect, manifests closure or has PACG itself. This is the first step of management. Then, a methodical distinction among a variety of anatomical and pathophysiologic mechanisms at play in the presenting eye must be evaluated. Hence, a mechanism-based scheme complements the diagnostic definitions; together they illuminate the natural history and stage-appropriate findings, which require intervention. When the outflow capacity of the angle is sufficiently compromised to elevate the IOP, possible irreversible damage to the optic nerve can subsequently ensue. Asymptomatic disease of presumably long duration is much more common than the dramatic symptoms of a precipitous closure of the angle with rapid deterioration in optic nerve and/or corneal function. Acute PACG is a distinctive form of clinical disease with a constellation of presenting signs and symptoms requiring urgent intervention as well as preventive measures for the fellow eye. Most attacks of angle-closure glaucoma are unilateral. However, 5-10% of the attacks may affect both eyes simultaneously.

The three pathophysical mechanisms grouped in the consideration of PACG are:

1. Pupillary block glaucoma.
2. Plateau iris: configuration and syndrome (ciliary body anomalies).
3. Phacomorphic glaucoma (lens-induced obstruction).[6]

Pupillary block is the fundamental mechanism underlying the spectrum of PAC disease. Its pathophysiology involves:

1. Lens - iris apposition at the pupil with resultant bowing forward of the peripheral iris as aqueous pressure builds up in the posterior chamber.
2. An anatomically predisposed eye that allows the anterior displaced peripheral iris to occlude the trabecular meshwork.

The distinction between an acute attack and chronic disease remains important for clinical management decisions. The management of PACG includes lowering of intraocular pressure by drugs, intensive pilocarpine therapy and topical, oral and systemic antiglaucoma medications. Laser intervention with an Nd-YAG peripheral laser iridotomy helps in relieving the pupillary block and opening of the angle and facilitating the aqueous outflow.

The fellow eye should also be examined and if deemed occludable, our recommendation is to proceed with iridotomy on both eyes at the same sitting. Prophylactic laser iridotomy plays a key role in the initial stages of the disease and acute angle closure attack can be averted. Acute angle closure glaucoma not only decompensates the cornea, but also affects visual prognosis by optic nerve damage. Though pressure reduction is achieved by various surgical modalities, the visual outcome is affected because of the reduction in the endothelial cell count by compromising the corneal clarity.

In our study, the fellow eyes without acute angle closure attack had an average endothelial count of 2615 cells/mm2. The eyes with acute angle closure attack had an average count of 2104 cells/mm2. Out of these, those patients who presented <72 hours, average count was 2252 cells/mm2, and those who presented >72 hours average count was 1861 cells/mm2. In our study, a significant reduction of corneal endothelial cell count by 20% was noted following an acute attack of angle closure glaucoma. The time of presentation of the patient from the onset of symptoms to seeking medical help may vary. The longer this duration of attack, the more the damage to the corneal endothelium. Bigar F.[7] et al found a decrease in endothelial count by 33% compared to fellow eye in the study done on 20 patients. The mean endothelial cell density in the affected eye was 1534 and in the unaffected fellow eye 2243 cells/mm2 in their study.

They concluded that decreased number of endothelial cells after an acute angle-closure glaucoma frequently combined with cornea guttata accounted for the corneal degeneration in these patients following a cataract extraction. Sihota R et al[8] studied endothelial status in various subtypes of glaucoma on 30 consecutive patients and reported a significant decrease in the corneal endothelial cell density in eyes with acute angle-closure glaucoma and chronic angle closure glaucoma. They found an increased pleomorphism and polymegathism of the corneal endothelial cells seen in eyes with resolved acute and chronic PACG.

Similar study done by Malaise-Stals J.[9] on 44 eyes of acute attack compared to 174 control eyes found a significantly decreased endothelial count following an acute attack. MJ Chen et al[10] also found that corneal endothelial cell density was significantly reduced in acute PACG eyes compared with normal eyes and noticed no significant difference in endothelial cell density of acute PACG eyes when compared with fellow PACG or chronic PACG eyes. They also concluded that corneal endothelial cell density was negatively associated with the duration of the acute attack. The mean endothelial cell density was 2271±80 compared to 2104 cells/mm^2 in our study.

Comparison of Our Study with Previous Published Data:

Studies	Endothelial Count (Cells/mm^2)
Present Study	2104
Bigar F et al[7]	1534
Sihota R et al[8]	1597±653
M J Chen et al[10]	2271±80
Han GH et al[11]	1758.67±794.33

The present study concerns the effect of acute attack of angle closure on corneal endothelial count and confirms other published data. Longer duration of attack showed a higher reduction of endothelial count. Up to 77% loss of cells is seen with longer attacks.[7] Sihota et al[8] study showed that eyes in which acute attack persisted for less than and more than 72 hours had an endothelial count of 2016±306 cells/mm^2 and 759±94.4 cells/mm^2, respectively. Melamed et al[12] conducted experiments on rabbit cornea and found that induced ocular hypertension produced morphologic changes in the endothelium possibly associated with decreased corneal endothelial density.

They showed that High IOP Affects the Cornea by Two Mechanisms:

1. High IOP affects the metabolic active pumping mechanism without any morphological changes, thus reducing resistance to aqueous flow to the stroma with resultant stromal oedema.
2. Elevated IOP causes morphological cellular damage, thus anatomically and functionally reducing the barrier to fluid flow into the stroma.

The decrease in endothelial count warrants a meticulous cataract and trabeculectomy surgery with least possible surgical trauma and adequate intraoperative modifications like using high molecular weight viscoelastics, low power settings in phacoemulsification, etc. The complications associated with this condition following surgery like corneal oedema, bullous keratopathy to be borne in mind and adequate precautions to be taken to preserve the quality of vision.

CONCLUSION: Corneal endothelial cell density was found to be reduced following an acute attack of angle closure glaucoma and correlates with duration of attack. Due care to be taken intraoperatively when surgical intervention planned. Due to the advent of newer diagnostic modalities and increasing awareness about glaucoma among the medical fraternity, the incidence of acute angle closure glaucoma has reduced. However, still few patients do present with acute attacks due to lack of prior ophthalmic examination or the attack maybe the first, which is severe.

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