

## Alterations in Specular Microscopy Following Combined Phacotrabeculectomy with MMC and Phacoemulsification

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**Abstract:** The corneal transparency is maintained by the Na<sup>+</sup>/K<sup>+</sup>-ATPase pump of the endothelial cells. This pump function is affected following intraocular surgery due to endothelial cell loss. The purpose of this study was to evaluate and compare the pre-operative and post-operative changes in specular microscopy following combined Phacotrabeculectomy with MMC (Group A) versus Phacoemulsification (Group B). Sixty eyes were included in both the groups. Post-operatively there was a significant reduction in the endothelial cell density and a corresponding increase in Coefficient of Variation in both the groups. A significant reduction was noted in CCT of Group A and no such change was seen in Group B in the post-operative period. This difference in post-operative CCT could be related to the drop in IOP in subjects of Group A.

**Keywords:** Specular microscopy, central corneal thickness, endothelial cell loss

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### I. Introduction

Corneal endothelium is comprised of a single layer of hexagonal cells which keeps the cornea in a dehydrated state due to its Na<sup>+</sup>/K<sup>+</sup>-ATPase pump activity, thereby maintaining its transparency.<sup>1</sup> The endothelial cell density (ECD) is highest at birth and steadily declines with age. In adults it ranges from 2500 to 3000 cells/mm<sup>2</sup>. ECD lesser than 400-500 cells/mm<sup>2</sup> leads to corneal decompensation and there is a resultant loss of vision.<sup>2</sup> Severe cell loss is noted following trauma, intraocular surgeries especially in hard cataracts, longer surgical time, based on surgical technique, and adjunctive use of antimetabolites like Mitomycin C (MMC).<sup>3,4</sup> The endothelium is amitotic and the cell loss is compensated by pleomorphism and polymegathism of the residual cells along with a transient increase in central corneal thickness (CCT) due to corneal edema.

Various techniques are available to study the corneal endothelium. Specular microscopy is a non-invasive imaging modality to study the endothelial cell morphology. Other parameters such as cell density, coefficient of variation (CV), percentage of hexagonality, central corneal thickness can also be analysed by specular.

### II. Material And Methods

This is a prospective study conducted at a tertiary eye care centre in South India from January 2018 to January 2019. The purpose of the study was to evaluate and compare the pre-operative and post-operative changes in specular microscopy following combined phacotrabeculectomy with MMC (Group A) versus phacoemulsification (Group B). Sixty eyes were included in each group after taking their informed consent. The surgeries were performed by a single surgeon. Specular microscopy of the central cornea was taken using TOMEY EM-3000 non-contact specular microscope by a single technician both in the pre-operative as well as in the three months post-operative follow-up period.

**SUBJECTS:** Patients with all types of glaucoma (primary open angle glaucoma, primary angle closure glaucoma, pseudoexfoliative glaucoma, normal tension glaucoma) along with clinically significant cataract not responding to maximal medical therapy, were enrolled into Group A to undergo combined phacotrabeculectomy with adjunctive MMC.

Patients who were glaucoma suspects with clinically significant cataract requiring cataract surgery were enrolled into Group B. Glaucoma suspects were defined as patients with IOP in the range of 21-25 mmHg or disc suspects with normal visual fields and optical coherence tomography (retinal nerve fibre layer), not requiring filtering surgery.

**Exclusion criteria:**

1. Patients with pre-existing corneal diseases
2. Patients who had undergone previous intraocular surgery
3. Intraoperative complications leading to prolonged surgical time like posterior capsular rent, vitreous loss
4. Postoperative shallow anterior chamber

**SURGICAL TECHNIQUE:**

All the subjects were operated by a single surgeon. Group A subjects underwent a twin site combined phacoemulsification with trabeculectomy surgery and intraocular lens (IOL) implantation. Intraoperatively MMC 0.02% sponge was applied subconjunctivally over the scleral flap for two minutes and then irrigated with copious amounts of Balanced Salt Solution. Group B subjects underwent temporal clear corneal phacoemulsification along with IOL implantation. Antibiotic with steroid preparation along with NSAID topical eye drops were given for a duration of six weeks in the post-operative period.

**Statistical analysis:** SPSS software for Windows version 17.0.0 (IBM Corp., Armonk, NY) was used for statistical analysis. All values were expressed as Mean±Standard deviation (SD). Data was checked for normality and paired t-test was used for intragroup comparison of pre-operative and post-operative mean values. Independent t-test was applied for comparison between the mean values of Group A and Group B. A p-value of 0.05 or less was considered statistically significant.

**III. Result**

Sixty eyes of 45 patients were included in Group A (combined phacotrabeculectomy with MMC) of which 24 were males and 21 were females. 60 eyes of 49 patients were included in Group B (Phacoemulsification) of which 27 were males and 22 were females. The mean age for Group A was 67.8±8.01 years and Group B was 62.9±7.61 years.

The mean pre-operative endothelial cell density (2532.48±238.88 cells/mm<sup>2</sup> vs 2547.42±226.17 cells/mm<sup>2</sup>) and coefficient of variation (36.53±5.22% vs 36.86±5.08%) of the two groups were comparable. However the mean pre-operative central corneal thickness of Group A was higher than that of Group B (528.06±48.95 μm vs 504.4±30.83 μm) and this was found to be statistically significant (p=0.01).

Patients in both the groups had a significant ECD loss in the post-operative period, although it was much higher in Group A (15.8% vs 11.15%). In both the groups, ECD loss was lesser for patients with Grade two cataract (13.42% in Group A vs 8.89% in Group B) than with Grade three cataract (17.7% for Group A vs 13.6% for Group B). CV increased by significant amount in both the groups. CCT decreased significantly (p=0.03) following surgery in Group A from 528.06±48.95 μm to 518.2±50.85 μm. On the other hand CCT remained almost the same 504.4±30.83 μm to 505.72±29.64 μm in Group B.

Patients in Group A had a clinically significant drop in intraocular pressure (IOP) following surgery (p<0.05) from 22.95±6.06 mmHg to 14.07±3.52 mmHg, whereas no significant change (16.55±1.76 mmHg to 15.35±1.93 mmHg) in IOP was noted in Group B. Both groups had a clinically significant improvement in visual acuity in post-operative period.

	Group A		Group B	
	Pre-operative	Post-operative	Pre-operative	Post-operative
ECD	2532.48±238.88 cells/mm <sup>2</sup>	2133.08±443.55 cells/mm <sup>2</sup>	2547.42±226.17 cells/mm <sup>2</sup>	2263.98±398.36 cells/mm <sup>2</sup>
CV	36.53±5.22%	38.81±5.65%	36.86±5.08%	38.13±3.81%
CCT	528.06±48.95 μm	518.2±50.85 μm	504.4±30.83 μm	505.72±29.64 μm

**IV. Discussion**

Endothelial cell damage is an unavoidable consequence of any intraocular surgery, be it phacoemulsification or combined phacotrabeculectomy. Factors like phacoemulsification time, phaco power, surgical time, grade of cataract, size of the incision, fluidics, trauma due to instrumentation or IOL contact, use of adjunctives like MMC can further affect the loss of endothelial cells. In our study the mean pre-operative ECD was 2532.48±238.88 cells/mm<sup>2</sup> in Group A and was comparable to that of Group B, 2547.42±226.17 cells/mm<sup>2</sup>, both of which fell within normal cell range for adults (2500-3000 cells/mm<sup>2</sup>). ECD values following three months of surgery in Group A was found to be 2133.08±443.55 cells/mm<sup>2</sup> and 2263.98±398.36 cells/mm<sup>2</sup> in Group B. Thus the endothelial cell loss (ECL) was statistically significant and was 15.8% in Group A (p<0.05) vs 11.15% in Group B (p<0.05), which show a correlation with other studies. The higher ECL in Group A could be attributed to the adjunctive use of MMC. Nader Nassiri et al in their study of comparison of corneal endothelial cell changes after 1-Site and 2-Site phacotrabeculectomy showed a mean ECD loss of 15.7% ± 2.8%<sup>5</sup> whereas Romeo Altafini et al showed a mean ECD loss of 12.3±8.9%<sup>6</sup>. Literature search showed that the range of ECD loss following phacoemulsification fell between 4% and

17.5%.<sup>7,8</sup>Shahram Bamdad et al reported a 11.4% ECD loss following phacoemulsification in their study.<sup>9</sup>In the three months post-operative period Reuschel et al found a 4.5-7.9% loss in ECD.<sup>10</sup>

Due to the lack of regenerative capacity of endothelial cells following ECL, the cornea recovers by cell enlargement and the remaining cells slide across to fill in the spaces which leads to an increase in Coefficient of Variation,<sup>11</sup> as it gives an objective measure of polymegathism.<sup>12</sup>A statistically significant increase in CV was noted in both the groups in our study. Group A showed an increase in CV from 36.53±5.22% to 38.81±5.65% (p=0.0004) and CV of Group B also increased from 36.87±5.08% to 38.13±3.81% (p=0.03). Although CV increased from 33.9±1.6% to 34.1±1.2% in a study conducted by Stéphane Arnavielle et al<sup>12</sup>, and from 27.38 ± 4.55% to 28.35 ± 4.47% in a study conducted by Anand et al,<sup>13</sup> neither of them were statistically significant.

As filtration surgery was done in Group A, there was a significant drop in IOP (p<0.05) from 22.95±6.06mmHg to 14.07±3.52mmHg. There was no change in IOP noted in Group B. Clement et al showed a significant drop in IOP in their combined phacotrabeculectomy patients,<sup>14</sup> from 23.8±4.3 mmHg to 14mmHg. Brian Song et al<sup>15</sup> in their one year follow up of phacotrabeculectomy found a significant reduction in IOP from 21.3±7.9mmHg to 12.2±3.9mmHg. Mustafa Kamal Junejo et al also similarly showed a statistically significant drop in IOP from 25.4 ± 8.0 mmHg to 12.9 ± 4.0mmHg.<sup>16</sup>

Many studies have proved that moderate amounts of surgical trauma induced to the corneal endothelium leading to ECL results in transient increase in CCT due to corneal edema.<sup>17</sup>This increase in CCT is noted mainly in the immediate post-operative period. However the CCT returns to pre-operative values within three months post-operatively. In our study this consensus has been followed in Group B as the CCT values showed no significant changes (504.4±30.83µm to 505.72±29.64µm). These findings were also noted in Sobottka Ventura et al<sup>17</sup> study who had shown no significant changes in the post-operative CCT (537±27µm to 539±28µm). Thus proving that when healthy endothelial cells remain in the normal cell count range there is no significant and persistent increase in CCT. Also, higher pre-operative CCT values were noted in Group A (528.06±48.95µm) in comparison to Group B (504.4±30.83µm) which was found to be statistically significant (p=0.01). This could be possibly explained by a higher pre-operative IOP values in Group A. Post-surgery the CCT values in Group A reduced to 518.2±50.85µm which could be attributed to the significant IOP reduction. A study conducted by Mustafa Kamal Junejo et al also showed a decrease in CCT (524.25 ± 38.53 µm to 521.95 ± 38.25 µm) although they did not find it to be statistically significant. As the functioning capability of endothelial cells is adequate for minimal to moderate amounts of ECL, the change in the CCT is probably not related to the depletion in the endothelial cell count. This can be seen in our study as there was a higher ECL (15.7%) in Group A, yet there was a decrease in the CCT. Another hypothesis could be that the endothelial pump mechanism becomes more efficient due to reduction in IOP, hence bringing about a reduction in CCT in combined phacotrabeculectomy patients.

## V. Conclusion

As seen in our study the pre-operative ECD of both the groups were comparable and fell within the normal cell count range. A higher ECL was noted in Group A and has been attributed to the adjunctive use of MMC. The higher pre-operative CCT in Group A could be explained by their higher pre-operative IOP values. High IOP hampers the functional capabilities of the endothelial cell pump to maintain the cornea in its dehydrated state which probably explains the thicker corneas in Group A. Similarly in the three months post-operative period the filtering surgery in Group A brought about a significant IOP reduction and a significant CCT reduction. Thus again emphasizing on the probable involvement of IOP levels affecting the functioning of the endothelial pumps. This may not be related to ECL as a higher ECL was noted in Group A. After a drop in IOP, the remaining endothelial cells would have been functioning better than their pre-operative state thus bringing about a drop in CCT.

Drawbacks of the study were that we were unable to analyse the effects of antiglaucoma medications on corneal endothelium in Group A patients. Further studies involving higher patient numbers and longer post-operative follow up period will be needed.

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