Comparison of corneal endothelial cell loss during phacoemulsification using continuous anterior chamber infusion versus those using ophthalmic viscosurgical device: Randomized controlled trial

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Aim: We conducted this study to evaluate and compare corneal endothelial cell loss between phacoemulsification with continuous anterior chamber infusion using anterior chamber maintainer (ACM) and phacoemulsification using ophthalmic viscosurgical device (OVD).

Materials and Methods: This was a prospective, randomized controlled trial. Fifty eyes of 47 patients of senile cataract undergoing phacoemulsification were included. Patients were randomly allocated into two groups of 25 eyes each. Cataract surgery was performed by phacoemulsification with anterior chamber (AC) continuous infusion with balanced salt solution (BSS) plus and ACM without OVD in Group A, and in Group B, phacoemulsification was performed using OVD with BSS plus. Corneal endothelial cell count and pachymetry were performed preoperatively and postoperatively on day 1, day 7, and day 30.

Results: The mean increase in pachymetry was 4.86%, 2.94%, and 1.94%, (Group A) and 5.95%, 3.94%, and 0.51%, (Group B) on first, seventh, and 30th postoperative day respectively. The difference between the percentage increase in pachymetry between the two groups was not significant at day 1 (P = 0.441), day 7 (P = 0.298), and day 30 (P = 0.174) postoperatively. The density of endothelial cells decreased postoperatively (day 30) by 7.38% (Group A) and 7.47% (Group B) without any significant statistical difference (P = 0.983) between two groups.

Conclusion: Use of ACM for continuous AC infusion and omission of OVD during phacoemulsification did not cause significant difference in corneal swelling or endothelial cell loss in the immediate postoperative period up to one month.

Key words: Anterior chamber maintainer, balanced salt solution plus, corneal endothelium, ophthalmic viscosurgical device, pachymetry, phacoemulsification


In early studies, phacoemulsification was associated with 16–67% endothelial cell loss correlating with the degree of trauma during surgery.[11] Various causes have been attributed for endothelial damage.[12–14] Balanced salt solution plus (BSS plus) is safe for intraocular irritation.[15–17] Ophthalmic viscosurgical devices (OVDs) are used to maintain the anterior chamber (AC) and also to coat the endothelium during cataract surgery.[18] Conversely, some OVDs have been shown to increase thermal damage causing endothelial cell loss.[19] OVDs may also cause increase in the intraocular pressure (IOP) and inflammation in the immediate postoperative period, which may cause further endothelial cell loss.[20] Anterior chamber maintainer (ACM) has been used to maintain the chamber during cataract surgery and thus reduce endothelial cell loss.[21] It may obviate the need for an OVD and thus prevent the problems inherent with OVDs. There are no data about the endothelial cell loss in phacoemulsification surgery with ACM without the use of OVDs available in literature. The aim of the study was to evaluate and compare the endothelial cell loss in phacoemulsification with ACM without OVDs when compared with that in phacoemulsification with OVDs alone in the immediate postoperative period in patients with senile cataract.

Materials and Methods

A randomized controlled trial was conducted in a tertiary-care, multidisciplinary hospital in western India between November 2005 and October 2006 on 50 eyes of 47 patients of senile cataract. All patients were informed and a written consent was obtained from them to participate in the study. Inclusion criteria were age between 40 and 80 years, senile cataract, and nucleus sclerosis up to grade 3. Exclusion criteria were any evidence of subluxation or pseudoxefoliation, any other associated ocular pathology, history of previous ocular surgery, corneal pachymetry greater than 630 µm, preoperative endothelial count less than 1500 cells/mm², pupil size less than 7.5 mm after dilatation, AC depth less than 2.25 mm, complicated cataract, previous history of laser (lasik or panretinal photocoagulation), diabetic retinopathy, and preoperative diagnosis of glaucoma and/or IOP greater than 20 mmHg. Other intraoperative exclusion criteria were total surgical time of more than 15 min, total phaco time of more than 90 s, effective phaco time of more than 10 s, average ultrasound (US) power > 30%, and...
any intraoperative complications. The history was recorded using a prefixed questionnaire that included information on age, sex, duration of decrease in visual acuity, and presence of any systemic diseases such as hypertension, diabetes mellitus, and ischemic heart disease. Preoperative evaluation of the patients included the measurement of uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA), an examination of the anterior segment of the eye under slit lamp biomicroscope, central corneal thickness and fundus evaluation through a dilated pupil. Grading (0 to 4+) of the nuclear sclerosis (a combination of opalescence and yellowing) was performed on slit lamp biomicroscope according to Emery and Little nuclear hardness classification. Intraocular pressure was recorded preoperatively with Goldmann applanation tonometer in all the patients. Keratometry was performed using Auto-Kerometer (Nidek KM-500), while the axial length and AC depth was measured using standard A-scan machine (Axis II, Quantel Medical) using the immersion technique. The power of the intraocular lens (IOL) was calculated in all the patients using SRK-T (Sanders, Retzlaff, Kraft) formula. Central corneal pachymetry and central corneal endothelial cell density were determined by SP-2000P noncontact specular microscope (Topcon America Corporation, Paramus, NJ). The selected patients were divided in two groups:

Group A (ACM Group, n = 25): Cataract surgery was performed by phacoemulsification with AC continuous infusion with BSS plus solution (Alcon Surgical, USA) using ACM without OVD.

Group B (OVD Group, n = 25): Cataract surgery was performed by phacoemulsification with OVD 1% sodium hyaluronate (Hyvisc-Sun Pharmaceuticals Ltd.) used with BSS plus solution.

In both groups, central corneal pachymetry and corneal endothelial count was assessed preoperatively and on postoperative day 1, day 7, and day 30.

Randomization was done preoperatively by the statistical random table. Surgery was performed by a single surgeon (BKN) who was informed (after opening the sealed envelope) on the operation table about group allocation. Those examiners who performed postoperative examinations were masked about the group of the subject.

Surgical technique

Ofloxacin eye drops 0.3% (Ocuin-Sun pharmaceuticals) was instilled at 6-hourly intervals in the eye to be operated, from two days prior to surgery. All patients were given 1 gm of cephalozin intravenous (IV) injection in the operating room half an hour before surgery. Tropicamide with phenylephrine eye drops were used for preoperative pupillary dilatation. Surgeries were performed under peribulbar anesthesia using 2 mL of 0.5% bupivacaine and 4 mL of 2% lignocaine mixed with 150 IU of hyaluronidase. Surgery was done using Millennium (Bausch and Lomb, NY, USA) phacoemulsification machine with CSS software. Two side-port ab-externo incisions, one at 10:30 position and another at 2:30 position were made with a 20-gauge MVR blade. A third incision was made for the ACM at 6 o’clock position with a 20-gauge microvitrecotinal (MVR) blade. In Group A, ACM was introduced in bevel down position with the flow being on, and in Group B, the AC was filled with OVD (1% sodium hyaluronate). Capsulorrhesis was performed by a bent tipped 26G cystitome under continuous AC infusion in Group A and with OVD in Group B. A triplaner corneal tunnel incision starting at mid limbus was made with a 2.75 mm angled slit knife (Alcon surgical, USA) under continuous AC infusion in Group A and under OVD in Group B. Hydrodissection and hydrodelineation were performed to achieve free rotation of nucleus. Phacoemulsification was done using quick chop technique. In Group A, this step was performed under continuous AC infusion, and in Group B, this step was performed under OVD. The following phaco parameters were used: 15-degree Millennium phaco tip, maximum vacuum 400 mmHg, maximum US power 25%, duty cycle 60%, bottle height 60 cm above the patient’s eye, and CSS software with waveform bursts. Cortical aspiration was done in both groups with the help of ACM with a special aspiration cannula controlled manually through an attached 5-mL disposable syringe. The foldable lens, single piece hydrophilic acrylic lens (Forelens, Hanita, Israel) was implanted by injecting through the viscojet cartridge attached to a titanium injector in all patients. In Group A, the IOL was inserted under the continuous infusion with ACM and in Group B, the AC and the capsular bag were filled with OVD. After IOL implantation OVDs were removed thoroughly. All the entries were hydrated at the end of the surgery. Subconjunctival injection consisting of 0.5 ml gentamycin (40 mg/mL) and 0.5 mL dexamethasone (4 mg/mL) was given. Postoperatively, patients were prescribed tobramycin + dexamethasone eye drops and ofloxacin eye drops 0.3% six times daily in reducing frequency for four weeks and tropicamide and phenylephrine eye drops two times per day for one week. The intraoperative parameters recorded were the group name, total phaco time, effective phaco time, average US energy used, and total surgical time. Pachymetry readings were considered only when the cell borders appeared well defined on the monitor. The endothelial cell density was then determined by manual counting of 70 cells after freezing the image on the screen (variable frame analysis). Three such readings were taken and their mean was recorded.

Statistical analysis

SPSS version 12 was used for data analysis. The preoperative data obtained in both the groups were analyzed for similarity. Estimates of correlation were obtained between the different parameters and postoperative increase in pachymetry on day 1 and also with the decrease in endothelial cell counts at 30 days. Paired t tests were performed to compare the postoperative corneal thickness and endothelial cell counts with the preoperative levels and also to compare between the two groups.

Results

The age range was from 41 to 80 years. The mean age of Group A was 61.44 ± 7.68 and of Group B was 63.36 ± 10.27. There were 12 male and 13 female patients in both groups. There were no significant differences in various preoperative parameters between Group A and Group B [Table 1]. The mean amount of BSS plus used in group A was 220.40 ± 82.08 mL and in Group B was 149.60 ± 55.36 mL (P = 0.001). More amount of BSS plus used in group A was due to continuous irrigation even at the time of capsulorrhesis and hydro procedures, which was performed under OVD in group B.
Table 1: Patient demography

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A</th>
<th>Group B</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Preoperative endothelial cell count (cells/mm²)</td>
<td>2796.64</td>
<td>303.97</td>
<td><strong>0.475</strong></td>
</tr>
<tr>
<td>Preoperative pachymetry (µm)</td>
<td>514.16</td>
<td>34.45</td>
<td></td>
</tr>
<tr>
<td>Total phaco time (s)</td>
<td>44.64</td>
<td>18.99</td>
<td></td>
</tr>
<tr>
<td>Effective phaco time (s)</td>
<td>3.76</td>
<td>2.44</td>
<td></td>
</tr>
</tbody>
</table>

*Level of significance. **Standard deviation

In this study, there was an increase in pachymetry of 4.86% and 5.95% on the first postoperative day in Group A and Group B, respectively [Table 2]. The difference was significant in both groups compared with the preoperative values (P < 0.001), the difference between the percentage increase in pachymetry between the two groups was not significant (P = 0.441). Seven days postoperatively, the increase in pachymetry differed significantly from the preoperative values in both groups, but the difference in percentage increase between the two groups was not statistically significant (P = 0.13). At 30 days, the percentage increase in pachymetry was still significant (P = 0.018) in Group A but was not significant for Group B (p = 0.361). However, the P value for the comparison between the two groups was not significant (P = 0.174).

The endothelial cell counts preoperatively and at 30 days postoperatively are depicted in Table 3. The density of endothelial cells decreased postoperatively (day 30) by 7.38% (Group A) and 7.47% (Group B). There was no significant difference (P = 0.983) in endothelial cell loss between Group A and Group B at day 30.

### Discussion

Corneal endothelial damage during cataract surgery is a major concern for all ophthalmologists. Older age, small pupil diameter, high nucleus grade, large nucleus, greater infusion volume, type of IOL, greater amount of total emitted US energy, and longer duration of surgery are associated with endothelial cell loss.[14-16] We tried to control these factors by appropriate methodology to reduce potential bias. As the mean age of patients in both groups were not significantly different (P = 0.458), the influence of age was eliminated. Perez et al.[17] found increased endothelial cell loss with decreasing pupillary size.

### Table 2: Pachymetry in Group A and Group B on days 1, 7, and 30

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (um)</td>
<td>514.16</td>
<td>539.48</td>
</tr>
<tr>
<td>SD</td>
<td>34.45</td>
<td>47.40</td>
</tr>
<tr>
<td>Mean change (um)</td>
<td>25.32</td>
<td>15.72</td>
</tr>
<tr>
<td>SD</td>
<td>23.43</td>
<td>18.66</td>
</tr>
<tr>
<td>% change</td>
<td>4.86</td>
<td>2.94</td>
</tr>
<tr>
<td>SD</td>
<td>4.41</td>
<td>3.39</td>
</tr>
<tr>
<td>P value</td>
<td>&lt; 0.001*</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

*Significance, P value for comparison between Group A and Group B 0.448 on postoperative day 1, 0.298 on postoperative day 7, 0.174 on postoperative day 30

### Table 3: Endothelial cell count in Group A and Group B at 30 days

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Preoperative cell count</th>
<th>Cell count at 30 days</th>
<th>Comparison between Group A and Group B (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (cells/mm²)</td>
<td>2796.64</td>
<td>2580.00</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>303.97</td>
<td>432.27</td>
<td></td>
</tr>
<tr>
<td>Mean change (cells/mm²)</td>
<td>216.64</td>
<td>217.44</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>415.07</td>
<td>346.16</td>
<td></td>
</tr>
<tr>
<td>% change</td>
<td>7.38</td>
<td>7.47</td>
<td>0.983</td>
</tr>
<tr>
<td>Paired t #/ SD</td>
<td>2.61</td>
<td>3.14</td>
<td></td>
</tr>
<tr>
<td>Paired t # P value</td>
<td>0.015*</td>
<td>0.004*</td>
<td></td>
</tr>
</tbody>
</table>

*Test of significance. **Significance
However, we excluded pupils less than 7.5 mm in diameter, thus eliminating a potential factor that could have influenced the results. Studies have shown increased endothelial cell loss with increasing grades of nuclear sclerosis.[19] In our study, the two groups had almost equal grades of cataract. In addition, all cataracts with grade 4 nuclei were excluded.

The surgeon noted certain advantages of using ACM during the surgery. Capsulorrhexis in all the cases in the present study had been performed with a 26-G cystitome. The surgeon observed that the ease of capsulotomy was more with the AC infusion (Group A). This was because of the floating flap due to the continuous infusion, and hence the visibility was better as it was not lost in the cortical matter pulled up with the flap. Reduction of AC depth due to the egress of OVD out of the eye led to the capsulorrhexis moving to the periphery in some cases resulting in larger than planned capsulorrhexis in those cases in Group B, and the advancing edge was, at times, difficult to visualize as the flap got crumpled irregularly. All incisions were identical in both groups. In Group B, although eyeball volume was maintained but we noted soft eyeball with easily distortable cornea; therefore, it was difficult to maintain plane of incision during creation of the main incision. However, in Group A, using ACM, eyeball was firm, so that the desired plane of incision was maintained. In this study, total US time was similar in both groups ($P = 0.377$) and even the effective phaco time was not significantly different in both groups ($P = 0.377$), hence the influence of US time on endothelial cell loss was similar in either group. Introduction of IOL under ACM alone without OVDs was done in group A, which has been proven to be safe at six weeks by Shingleton et al.[19] We chose to use BSS plus in this study, as it has been noticed to cause less corneal edema immediately after intraocular surgery.[21] No significant differences in endothelial cell damage was noticed in patients that underwent phacoemulsification with four different OVDs: healon, amvisc plus occucoat (HPMC), and viscoat.[15,20] There was a significantly greater reduction in polymegathism in the healon group than in the viscoat group.[20] They concluded that the greater effort needed to remove viscoat from the AC may have adversely affected the endothelium. In our Group A, there was no effort for the removal of OVD involved because OVDs were not used at all. Healon appeared to have superior protective properties than HPMC at certain concentrations of hydrogen peroxide.[21] Because of this, we used sodium hyaluronate 1%.

All studies have used some form of OVDs in both their arms, but there was no study available in literature that compared OVD versus no OVD. The results of our study show that the corneal thickness returned close to preoperative values at one month in both groups with no significant differences between groups. We found an endothelial cell loss of 7.38% and 7.47% at one month in Groups A and B, respectively ($P = 0.983$). The values of endothelial cell loss are comparable with other studies. This proves that OVDs may not be necessary at all. Our study was limited by the fact that the follow-up period was of one month. Serial observations of the endothelium after the intraocular surgery have shown that the endothelium is in a state of transition for a long postoperative period with a progressive decline in cell density.[21]

It has already been proved that the endothelial cell loss during phacoemulsification is inversely proportional to the depth of the AC, and the ACM increases and maintains chamber depth through all stages of phacoemulsification. The use of ACM controls and stabilizes IOP at predetermined levels with minor fluctuations during phacoemulsification.[22,23] Chawla et al.[25] noted in their series that the AC was well maintained in all patients throughout the surgery; posterior position of the posterior capsule was maintained during irrigation/aspiration. Therefore, it should logically follow that the cell loss should be lesser with the use of ACM.

Milla et al.[26] compared the results of conventional phacoemulsification with and without continuous AC infusion used during nuclear phacoemulsification. They used continuous AC infusion only during nuclear phacoemulsification using continuous irrigation option through phaco probe. They used OVDs in both groups and found reduction in pachymetry at 30 days after an initial increase on day one in both groups. However, this reduction was more pronounced in the group with continuous AC infusion used during nuclear phacoemulsification. They found that the endothelial cell density had a steep drop in the continuous AC infusion group, which was significant at day 7, but the endothelial cell loss was not statistically different at day 30 between the two groups. In our study, we found no statistically significant difference at day 7 as well as day 30 in endothelial cell loss. However, we used ACM for continuous AC infusion in all stages of the surgery and noted other advantages, which were also noted by Milla et al.[26] Continuous AC infusion avoids intraoperative complications like AC collapse that can reduce the success of the surgery. Continuous AC infusion compensates for fluid losses through corneal incision. In the OVD group, we noted chamber collapse in seven patients, whereas it was not seen at all in the ACM group. Although the mean volume of BSS plus used in group A was significantly more than Group B, the endothelial cells loss was similar in both groups in our study.

In the present study, the use of ACM with apparently reduced cost due to the avoidance of OVDs did not alter the recovery of endothelial function in the short term (one month). Long-term evaluation was not done in this study. The OVDs, are expensive, did not give any significant advantage. However, this study was carried out on apparently normal corneas, so the results cannot be directly extrapolated to diseased corneas. Further studies using the same combinations on diseased corneas with low counts may help to determine whether the ACM with BSS plus without OVDs would actually be as effective in those situations compared with the use of OVDs. The other limitation of this study was that we did not record IOP at day one. It may have influence on pachymetry and further endothelial cell loss. The influence in both groups on visual rehabilitation and postoperative astigmatism needs to be evaluated in further studies.

**Conclusions**

As evident from the study, the omission of expensive OVDs did not cause a significantly different corneal swelling in the immediate postoperative period up to one month. The corneal endothelial cell loss at one month was 7.38% for the ACM
group without OVDs, and for the OVD group, it was 7.47% (statistically not significant). ACM gave definite advantages in terms of AC stability, lesser intraoperative complications due to loss of AC depth and ease of maneuverability.

References


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