Hydro-implantation versus Visco-implantation of Intraocular Lenses and Fluid Load Effect on Corneal Endothelial Cells after Uneventful Phacoemulsification

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Abstract

AIM: The purpose of the study was to study the effect of implantation method and fluid load (aspiration time, aspiration volume) on corneal endothelium in uneventful phacoemulsification surgeries.

METHODS: This study was a prospective and interventional study involved 77 eyes, 50–81 years, divided into three groups according to implantation method (on Saline, Healon, or Methylcellulose). Specular microscope analysis of corneal endothelial parameters: Cell density (CD), central corneal thickness (CCT), coefficient of variation (CV), and Hexagonality (HEX) were done before and 3 months after surgery.

RESULTS: A total of 77 eyes with cataracts were studied, and there was a significant increase in CCT and CV with a decrease in CD and HEX in all three groups. On comparing the same parameters between the three groups, there were insignificant differences regarding CCT and HEX changes. Although there was a significant change in CD, the highest loss was in the Healon group (median −0.138), followed by the Saline group (median −0.118), and the lowest was in the Methyl group (median −0.075). There was a significant change in CV, showing the highest increase in the Healon group (median 0.16129) followed by the Saline group (median 0.13307) and the lowest in the Methyl group (median 0.1266). There was a non-significant change in all corneal parameters among cases in each group with different aspiration volumes and times.

CONCLUSION: Endothelial cell loss was lowest with Methyl followed by saline, and highest with Healon implantation. Fluidics had an insignificant effect in the three groups. Saline implantation was comparable to Healon, with an insignificant difference in CD loss.

Introduction

The corneal endothelium is the cornea’s most posterior layer. It is a monolayer of uniformly shaped, polygonal squamous cells that are distributed uniformly throughout the cornea. The neural crest is formed during embryonic development [1], [2].

The loss of corneal endothelial cells, which do not divide, is only made up for by the remaining cells’ migration, expansion, and growing heterogeneity [3], [4].

Corneal endothelial cells provide an anatomical and physiological barrier between the anterior chamber and the corneal stroma. They maintain a 3.5–6 μL/h active fluid transfer from the stroma into the anterior chamber, regulating stromal hydration [5].

Corneal endothelial cells (CECs) are responsible for maintaining the cornea’s transparency, and endothelial dysfunction leads to visually disabling corneal edema. Modern phacoemulsification technologies have improved fluidics and decreased surge. In addition, modulation of parameters, such as interrupted phaco power, vacuum adjustments, and aspiration flow rates, have improved the safety and predictability of phaco surgeries [6], [7], [8], [9], [10].

Through its barrier and pump mechanisms, the corneal endothelium controls the outflow of aqueous humor (AH) to the stroma to maintain corneal transparency. However, due to their inactivity during the G1 phase of the cell cycle, corneal endothelial cells (CECs) are thought to have a restricted ability for regeneration in living organisms [11].

Investigations attributed the damage in the endothelium during phaco surgeries to many factors, including instruments, lens fragments, or an intraocular lens touching the endothelium [12], [13], [14]. Many studies and trials aimed at reducing corneal endothelial cell loss [15], [16], [17].

It is plausible to assume that individuals’ inherent hereditary characteristics, including CEC migration capacity, anterior segment configuration, and surgery-related parameters, may influence surgical results [3].
The amount of US energy and fluid flow within the anterior chamber is thought to influence the amount of damage to the corneal endothelium in the hands of skilled surgeons experienced in performing phacoemulsification [18].

While some surgeons like to use a high vacuum and flow rate to avoid the high amount of US energy generated in the eye and accelerate surgery, other surgeons use low parameters to reduce the traumatic effect of fluid turbulence [19].

Baradaran-Rafii et al. [20] compared low-vacuum and high-vacuum groups (200 mm Hg; flow rate of 20 cc/min and 400 mm Hg; flow rate of 40 cc/min, respectively). They found that the loss of endothelial cells was related to ultrasound energy rather than vacuum levels [20].

To the best of our knowledge, there is still a lack of peer-reviewed studies on the post-operative impact of fluidic load or quantity and method of IOL implantation on anterior segment structures. Therefore, we conducted a study to determine whether the implantation method or the amount of fluid load during phacoemulsification or had an impact on central corneal thickness (CCT) or corneal endothelial cell density (ECD).

Subjects and Methods

Ethical considerations

This study followed the instructions of the Al-Azhar Medical Research Ethical Committee and the Helsinki Declaration. All patients were counseled, and all subjects signed informed consent.

Study subjects

Patients with cataracts planned to do phacoemulsification and intraocular lens (IOL) implantation who agreed to be included in this study.

Patients had their preparations, examinations, and operations and followed up at Al-Azhar University Hospitals, Cairo, Egypt.

Inclusion criteria

Age-related cataract (nucleus grade I and II), clear cornea with no opacities, normal intraocular pressure, no retinal pathologies, normal appearance of the optic nerve head, and peri-papillary area were included in the study.

Exclusion criteria

Congenital cataracts, complicated cataracts, hard cataracts (Grades III and IV), known glaucomatous patients, history of intraocular or refractive surgery, previous eye trauma, history of uveitis, or chronic ocular medications were excluded from the study. Patients with operative or post-operative complications and those who failed to continue follow-up were also rolled out.

Assessment

Visual acuity assessment, slitlamp examination including biomicroscopy, examination of the pupil, and fundus examination were done for all subjects. IOP measurements using Goldmann applanation tonometer. All patients had a specular microscopic evaluation of the corneal endothelium, including central corneal thickness (CCT) [in um], cell density (CD) [cell/mm²], coefficient of variation in cell size (CV), and percentage of hexagonal cells (HEX). We used a non-contact specular microscope (Topcon® SP1-P, Tokyo, Japan) to examine the central corneal endothelium. Panorama mode allowed three images from the central cornea to be captured, and then combined to perform a wide analysis of the central corneal endothelium. A single examiner took all measurements under dim illumination 1 day before surgery, 3 months after surgery.

Surgical procedures

Pupils were dilated (using a combination of tropicamide 1% and phenylephrine HCl 2.5% eye drops) before surgery. The same surgeon did all surgeries with local anesthesia (M. Ibrahim). A 2.8-mm superior clear corneal stab incision was then followed by viscoelastic filling of the anterior chamber. First, about 6.0 mm capsulorhexis was first fashioned, then phacoemulsification (INFINITI_ vision system; Alcon, Novartis). Next, a mono-focal, foldable, hydrophilic, biconvex, and acrylic IOL (OculoFlex®, Eye Pharma, India) were implanted in the bag either using saline delivered by irrigation cannula or a viscoelastic: Either Methylcellulose (Optiflex®, hydroxypropyl Methylcellulose USP, 2.0% w/v, Moss Vision Inc, UK) or Healon (Optiflex®, Sodium hyaluronate EP 10mg/ml, Moss Vision Inc, UK). Finally, the corneal wound was sealed by hydration. The mean surgical time was 12.7 ± 2.8 min (range 8–17 min). Patients were then prescribed antibiotic (gatifloxacin 0.3%) and steroid (prednisolone acetate 1%) eye drops q.i.d for 4 weeks.

Statistical analysis

Statistical analysis was done by IBM SPSS statistics (V. 26.0, IBM Corp., USA, 2019) [21]. Data were explained as median and percentiles for quantitative, non-parametric data, in addition to both number and percentage for categorized data [22].
The following tests were used:

1. Wilcoxon Rank Sum test for comparison between two independent groups for non-parametric data.
2. Wilcoxon signed-rank test comparing two dependent groups for non-parametric data.
3. Kruskal Wallis test for comparison between more than two patient groups for non-parametric data.
4. Ranked spearman correlation test for correlation between non-parametric data.

The error probability at 0.05 was considered significant, while at 0.01 and 0.001 were considered highly significant.

Results

There was a highly significant increase in CCT and coefficient of variation and a decrease in CD and Hexagonality among cases in all three groups (Tables 1-3).

On comparing the same parameters between the three groups, there was no significant difference regarding changes in CCT and hexagonality. In contrast, there was a highly significant change in cell density (CD), showing the highest loss in Healon group (median -0.1388) followed by the saline group (median -0.1185) and lowest in the methyl group (median -0.0754). In addition, there was a significant change in the coefficient of variation (CV), showing the highest increase in Healon group (median 0.16129) followed by the Saline group (median 0.13307) and lowest in the Methyl group (median 0.1266) (Table 4).

There was a highly significant difference in aspiration volume among the 3 groups showing the highest increase in the Saline group (median 1.4 s), followed by Healon group (median 0.8) and the lowest in the methyl group (median 0.15 s). The rest of the parameters showed non-significant change (Table 5).

As we required more fluid volume for the Saline and methyl groups, we evaluated the effect of fluid load on the cornea: There was a non-significant change in all corneal parameters among cases in each group with different aspiration volumes and time (Tables 6-8). In addition, though the Saline group showed higher US time, both US time and torsion time had a non-significant effect on the cornea (Table 9).

On comparing Saline implantation to methyl implantation, there was a significantly more loss of endothelial cells and a highly significant aspiration volume with Saline (Table 10). On comparing Saline implantation to Healon implantation, there was a non-significant difference in loss of endothelial cells and still a highly significant aspiration volume with Saline (Table 11). In comparing methyl implantation to Healon implantation, there was a significant increase in CCT, a highly significant loss of endothelial cells with Healon, and a non-significant change in aspiration volume between the two groups (Table 12).

Implantation on saline causes significantly more endothelial cell loss than on Methyl and non-significant loss compared to Healon. Conversely, implantation on Healon causes more significant cell loss than Methyl (Tables 11 and 12).

Discussion

Damage to the corneal endothelium can result from many factors, including anything that touches the...
back of the cornea, such as phaco tip, lens debris, and IOLs. It was shown that dispersive viscoelastic has more effective protection and barrier effect from air bubbles than cohesive viscoelastic. Dispersive viscoelastic and mainly viscoat® are used because of the ability to remain in the anterior chamber even when exposed to irrigation–aspiration forces that can effectively remove cohesive OVDs. Viscoat® was shown to protect against air bubble damage during phacoemulsification because of its ability to remain on the corneal endothelium during this procedure [23], [24], [25], [26], [27], [28].

Theoretically, the ideal viscoelastic material should be easily removable from the anterior chamber by the end of surgery to prevent the possible post-operative spike of intraocular pressure and inflammation, which carries the risk of more endothelial cell damage [29].

Holzer et al. compared 5 viscoelastic: Healon5 (sodium hyaluronate2.3%), HealonGV (sodium hyaluronate 1.4%), OcuCoat, and Celoftal (hydroxypropyl Methylcellulose 2.0%), and Viscoat® (sodium hyaluronate 3.0%–chondroitin sulfate 4.0%), in 81 eyes and found that endothelial cell loss occurred in all five types, with the lowest in the Healon5 group, with no significant difference in IOP in all groups [30].

The authors described the hydro-implantation technique where they used OVD only during capsulorhexis and not in any other stage of cataract surgery. They compared the advantages and disadvantages of this technique [31], [32]. These studies found that OVD in cataract surgery was not indispensable.

Tak described the technique for hydro-implantation for inserting a foldable IOL without OVD. In his study, he compared hydro-implantation with visco-implantation and described that the depth of the anterior chamber and capsular bag were similar. There was no difference in corneal edema on the 1st post-operative day. A significantly less time was required for implantation of the lens in the hydro-implantation group (40–60s) compared to the visco-implantation group (2.4 to 4 min) [32].

In our study, we studied a total of 77 eyes with cataracts, aged 50–81 years, divided into three groups according to implantation method (Saline, Healon, or
Methylcellulose. All patients underwent uneventful phacoemulsification with IOL implantation in the bag. In addition, all patients had a full eye examination and specular microscopic analysis of corneal endothelial parameters (CD, CV, HEX, and CCT) before and 3 months after surgery. This was in accordance with the Oxford Cataract Treatment and Evaluation Team, which suggested that endothelial cell count should be performed at least 90 days postoperatively after stabilization of cell reorganization and loss. They reached this result after examining and following up on more than 300 eyes following cataract surgery for 4 years [33].

Table 6: Correlating changes in endothelial parameters for fluidic parameters in saline group (ranked spearman correlation test)

<table>
<thead>
<tr>
<th>Items</th>
<th>Aspiration volume</th>
<th>Aspiration time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>−0.135</td>
<td>0.53</td>
</tr>
<tr>
<td>CCT pre-operative</td>
<td>0.048</td>
<td>0.823</td>
</tr>
<tr>
<td>CCT post-operative</td>
<td>0.057</td>
<td>0.791</td>
</tr>
<tr>
<td>CCT dC</td>
<td>0.3</td>
<td>0.154</td>
</tr>
<tr>
<td>CD pre-operative</td>
<td>0.175</td>
<td>0.406</td>
</tr>
<tr>
<td>CD post-operative</td>
<td>0.137</td>
<td>0.523</td>
</tr>
<tr>
<td>CD dC</td>
<td>−0.121</td>
<td>0.574</td>
</tr>
<tr>
<td>CV pre-operative</td>
<td>−0.182</td>
<td>0.394</td>
</tr>
<tr>
<td>CV post-operative</td>
<td>−0.124</td>
<td>0.564</td>
</tr>
<tr>
<td>CV dC</td>
<td>0.186</td>
<td>0.384</td>
</tr>
<tr>
<td>HEX Pre-operative</td>
<td>0.154</td>
<td>0.472</td>
</tr>
<tr>
<td>HEX post-operative</td>
<td>0.075</td>
<td>0.729</td>
</tr>
<tr>
<td>HEX dC</td>
<td>−0.034</td>
<td>0.875</td>
</tr>
</tbody>
</table>

Hydroimplantation was tried on 100 eyes having pseudoxefoliation syndrome by Öğurel et al. [32] to reduce IOP changes and surgical time.

Table 7: Correlating changes in endothelial parameters for fluidic parameters in methyl group (ranked spearman correlation test)

<table>
<thead>
<tr>
<th>Items</th>
<th>Aspiration volume</th>
<th>Aspiration time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.054</td>
<td>0.822</td>
</tr>
<tr>
<td>CCT pre-operative</td>
<td>−0.308</td>
<td>0.915</td>
</tr>
<tr>
<td>CCT post-operative</td>
<td>0.043</td>
<td>0.859</td>
</tr>
<tr>
<td>CCT dC</td>
<td>0.135</td>
<td>0.571</td>
</tr>
<tr>
<td>CD pre-operative</td>
<td>0.079</td>
<td>0.742</td>
</tr>
<tr>
<td>CD post-operative</td>
<td>−0.002</td>
<td>0.828</td>
</tr>
<tr>
<td>CD dC</td>
<td>−0.128</td>
<td>0.591</td>
</tr>
<tr>
<td>CV pre-operative</td>
<td>0.296</td>
<td>0.205</td>
</tr>
<tr>
<td>CV post-operative</td>
<td>0.497</td>
<td>0.026</td>
</tr>
<tr>
<td>CV dC</td>
<td>0.293</td>
<td>0.21</td>
</tr>
<tr>
<td>HEX pre-operative</td>
<td>−0.012</td>
<td>0.096</td>
</tr>
<tr>
<td>HEX post-operative</td>
<td>−0.073</td>
<td>0.758</td>
</tr>
<tr>
<td>HEX dC</td>
<td>−0.021</td>
<td>0.93</td>
</tr>
</tbody>
</table>

We found a highly significant increase in CCT and coefficient of variation and a decrease in CD and hexagonality among cases in all three groups. When comparing the same parameters between the three groups, there was no significant difference among three groups regarding the change in CCT and hexagonality. However, there was a highly significant change in cell density (CD), showing the highest loss in Healon group (median =−0.1388), followed by the Saline group (median =−0.1185) and lowest in the methyl group (median =−0.0754). In addition, there was a significant change in the coefficient of variation (CV), showing the highest increase in Healon group (median 0.16129) followed by the saline group (median 0.13307) and lowest in the methyl group (median 0.1266). There was no significant change in all corneal parameters among cases in each group with different aspiration volumes and times.

No statistically significant difference was noted in IOP between the two groups, except for the 1st 24 h post-operatively, where the visco-implantation group showed higher IOP than the hydro-implantation one (p = 0.035). Total surgery time was shorter in Group 1 compared to Group 2 because of the time needed for I/ A of Visco in Group 1 (p < 0.001). Better fixation of the globe during IOL implantation was another suggested advantage of hydro-implantation due to fixation by I/ A. It is also safer in toxic IOLs, where surgeons will not aspirate Visco from behind IOLs with less chance for rotation. No statistically significant differences in CCT and CD between both groups at each visit [34]. This was different from our results, but we did not include cases of pseudoxefoliation syndrome in our study.

Table 8: Correlating changes in endothelial parameters for fluidic parameters in Healon group (ranked spearman correlation test)

<table>
<thead>
<tr>
<th>Items</th>
<th>Aspiration volume</th>
<th>Aspiration time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.218</td>
<td>0.233</td>
</tr>
<tr>
<td>CCT pre-operative</td>
<td>−0.234</td>
<td>0.19</td>
</tr>
<tr>
<td>CCT post-operative</td>
<td>−0.224</td>
<td>0.211</td>
</tr>
<tr>
<td>CCT dC</td>
<td>−0.08</td>
<td>0.66</td>
</tr>
<tr>
<td>CD pre-operative</td>
<td>−0.179</td>
<td>0.319</td>
</tr>
<tr>
<td>CD post-operative</td>
<td>−0.194</td>
<td>0.28</td>
</tr>
<tr>
<td>CD dC</td>
<td>−0.008</td>
<td>0.733</td>
</tr>
<tr>
<td>CV pre-operative</td>
<td>0.203</td>
<td>0.257</td>
</tr>
<tr>
<td>CV post-operative</td>
<td>0.097</td>
<td>0.593</td>
</tr>
<tr>
<td>CV dC</td>
<td>−0.175</td>
<td>0.331</td>
</tr>
<tr>
<td>HEX pre-operative</td>
<td>−0.116</td>
<td>0.521</td>
</tr>
<tr>
<td>HEX post-operative</td>
<td>−0.214</td>
<td>0.232</td>
</tr>
<tr>
<td>HEX dC</td>
<td>−0.021</td>
<td>0.93</td>
</tr>
</tbody>
</table>
We did not notice a difference in AC stability in all groups nor recorded AC reactions. Lee et al. [35] compared implantation on BSS to implantation on OVD and found no significant difference regarding endothelial cell loss, central corneal thickness, the incidence of anterior chamber reaction, myopic shift, and posterior capsule opacification. They suggested that implantation on BSS will be more useful in vitrectomized eyes with capsule opacification. We did not notice a difference in AC stability in all groups nor recorded AC reactions. Lee et al. [35] compared implantation on BSS to implantation on OVD and found no significant difference regarding endothelial cell loss, central corneal thickness, the incidence of anterior chamber reaction, myopic shift, and posterior capsule opacification. They suggested that implantation on BSS will be more useful in vitrectomized eyes with capsule opacification. 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One drawback of leaving OVD between the lens and the posterior capsule is capsular block syndrome [36], [37]. Sim et al. [38] used IOL side rocking (judders technique) for Visco removal from behind IOL to avoid the risk of posterior capsular tear [38].

One possible advantage of hydro-implantation is good IOL optic apposition to the posterior capsule, which increases the barrier effect to the central migration of lens epithelial cells [39].

Studeny et al. [31] compared the safety of implanting a single-piece, foldable intraocular lens
(IOL) using BSS versus OVD in 200 eyes and reported a non-significant difference in endothelial cell loss at 1 and 6 months. In addition, they reported no increase in operative or post-operative complications in using BSS compared to standard OVD use [31].

This suggests that methyl implantation is safer for those with compromised corneal endothelium, while in healthy corneas, hydroimplantation (more economical and faster) is equivalent to Healon implantation.

**Conclusion**

Corneal endothelial cell loss is lowest with implantation on methylcellulose, followed by implantation on saline, and highest on using Healon. Fluidics has an insignificant effect in the three groups. When comparing Saline implantation to Healon implantation, there was a non-significant difference in the loss of endothelial cells. Therefore, saline can be used as effectively as Healon in implanting IOLs with less lens rotation. Hydro implantation is equivalent to Healon implantation but still more traumatic to corneal endothelium than methyl implantation.

**References**


