Combined Descemet’s membrane endothelial keratoplasty, phacoemulsification and intraocular lens implantation in Fuchs’ dystrophy

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PURPOSE: To evaluate the feasibility and outcome of combined Descemet’s membrane endothelial keratoplasty (DMEK), phacoemulsification and intraocular lens (IOL) implantation in the management of concomitant endothelial disorder, shallow chamber and cataract.

SETTING: Clinical study at a tertiary referral center.

METHODS: Prospective, nonrandomized study that included eight eyes of eight patients with concomitant endothelial disease and advanced cataract. In a first group of eight consecutive eyes, combined phacoemulsification, IOL implantation and DMEK were performed. Grafts were inserted with an ICL injector, encapsulated within viscoelastic plugs. Femtosecond laser-assisted descemetorhexis was performed in one case. The main outcome measures were best spectacle corrected visual acuity (BSCVA), endothelial cell density (ECD) and intra- and postoperative complications.

RESULTS: The procedure was successful in 75% (6/8) of cases. Two required a secondary regraft due to complete graft detachment and late failure. At six months, mean ECD loss was 55.4±24.0%, with an absolute mean ECD of 1248.3±755.0 cells/mm². At six months, 100% (5/5) of patients with good visual potential reached BSCVA of ≥0.5, 80% (4/5) ≥0.8, and 60% (3/5) ≥1.0.

CONCLUSIONS: The combined triple procedure seems to be safe and effective in the management of cases with concomitant advanced Fuchs’ endothelial dystrophy, advanced cataract and shallow chamber. Endothelial cell density loss beyond six months remains under investigation.

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curvatures; thus phacoemulsification and intraocular lens (IOL) implantation followed by DSAEK, as a combined procedure, results in rapid visual recovery and a more predictable refractive outcome than a triple procedure involving PK.

The introduction of Descemet’s membrane endothelial keratoplasty (DMEK) is the latest major step forward. Originally described by Melles in 2006, DMEK has proven to be the technique that provides fastest complete visual rehabilitation in Fuchs’ endothelial dystrophy\(^6\). It has become our technique of choice for a combined EK and phacoemulsification procedure. Thus, we set out to evaluate the feasibility and outcome of combined DMEK, phacoemulsification and IOL implantation in the management of concomitant endothelial disorder, shallow chamber and cataract.

**PATIENTS AND METHODS**

In a first group of eight consecutive eyes of eight patients with concomitant endothelial Fuchs’ dystrophy, shallow chamber and advanced cataract, seven females and one male, ranging from 54 to 67 years of age (61.6 ± 5.2), underwent phacoemulsification, IOL implantation and DMEK in a single procedure. All surgeries were performed by a single surgeon (J.A.). Minimum follow-up was six months. Successful graft was defined as a clear cornea with improved visual acuity and reduced pachymetry beyond six months after surgery. The study was conducted with informed consent from all patients, and with approval from the institutional ethical committee; it adhered to the guidelines of the Declaration of Helsinki.

**Donor tissue**

Corneoscleral buttons were excised from donor globes obtained <36 hours post-mortem and stored in Optisol (Optisol-GS; Bausch & Lomb, Inc.; Irvine, CA, USA) storage medium at 4° Celsius for 2-3 days. Endothelial cell morphology and viability were evaluated by automated inverted microscope cell counter (Konan eb-10; Irvine CA, USA) and mean endothelial cell density was 2680 ± 414.7 cells/mm\(^2\). Ten days prior to surgery, corneoscleral rims were mounted endothelial side up

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**Table 1. Results of PHACO-DMEK**

<table>
<thead>
<tr>
<th>Case</th>
<th>Patient age (yrs /gender)</th>
<th>OD/OS</th>
<th>Surgical Indication</th>
<th>ACD (mm)</th>
<th>Preop. CCP(μm)</th>
<th>Preop. BSCVA</th>
<th>Implanted IOL type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>66F OS</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>2.09</td>
<td>626</td>
<td>0.2</td>
<td>SN60WF</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>67F OD</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>1.89</td>
<td>998</td>
<td>0.5</td>
<td>SN60WF</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>54F OS</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>2.42</td>
<td>715</td>
<td>0.5</td>
<td>SN60WF</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>67F OS</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>1.76</td>
<td>682</td>
<td>0.2</td>
<td>SN60WF</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>56F OD</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>2.75</td>
<td>640</td>
<td>0.3</td>
<td>SN60WF</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>62F OS</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>2.63</td>
<td>631</td>
<td>0.2</td>
<td>SN60WF</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>58F OD</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>2.78</td>
<td>579</td>
<td>0.5</td>
<td>SN60WF</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>62M OS</td>
<td>Fuchs ED grade III, advanced cataract</td>
<td>2.5</td>
<td>567</td>
<td>0.8</td>
<td>SN60WF</td>
<td></td>
</tr>
</tbody>
</table>

Overall average BSCVA and ECD at 6 months after Phaco-DMEK.

**ACD**, Anterior chamber depth; **BSCVA**, best spectacle corrected visual acuity; **CCP**, central corneal pachymetry; **DMEK**, Descemet’s membrane endothelial keratoplasty; **ECD**, Endothelial cell density; **Fuchs ED**, Fuchs’ endothelial dystrophy; **POP**, postoperative pachymetry; **n.a.**, not applicable

\(^1\)ECD is also given as Absolute ECD in cells/mm\(^2\) in parentheses.
on a Barron holder equipped with a suction cup under microscopic control under strict sterile conditions at the eye bank. Descemet’s membranes were stripped from posterior stroma with Kellman-McPherson forceps, with the aid of one-minute 0.006% trypan blue stain solution (Visionblue, D.O.R.C. International, Rotterdam, The Netherlands), and finally excised with a Barron 8.75 mm trephine (Katena; New Jersey, U.S.A.). Descemet’s rolls were then transferred with a 250 mm glass Pasteur pipette (VWR International, model 612-2297; Leicestershire; England) and preserved until implantation in TissueC (Alchimia; Padova, Italy) organ culture storage medium at 31 °C.

**Phacoemulsification technique**

In recipient eyes, a 2.2 mm scleral tunnelized incision was constructed and cohesive viscoelastic (Provise Plus, Alcon, USA) was used to fill the anterior chamber. A 5.5 mm continuous circular capsulorhexis was created with a pre-formed cystotome, and followed by hydrodissection, rotation and phacoemulsification (Infinity Ozil, Alcon Surgical; Fort Worth,TX, USA) of the nucleus. The main incision was then enlarged to 3.2 mm and a capsular tension ring (Morcher GmbH; Stuttgart, Germany) was implanted along with a posterior chamber Acrysoft natural SN60WF intraocular lens (Alcon; Fort Worth,TX, USA). All traces of viscoelastic material were then carefully aspirated and the incision enlarged to 4 mm with a pre-calibrated ophthalmic knife.

**DMEK technique**

Immediately afterwards, a 9.0 mm epithelial mark was made to outline the area of the planned Descemet’s membrane excision. The anterior chamber was filled with air though the side-port, while keeping the main incision closed (a temporary suture was occasionally needed at this stage). After scoring the receptor endothelium with an inverted Sinskey hook, a circular portion of Descemet’s membrane (DM) was stripped from the posterior stroma, so that a 9.0 mm descemetorhexis was created. In one case, capsulorhexis, lens fragmentation and descemetorhexis were assisted by a LensX femtosecond laser (Alcon; Fort Worth, TX, USA).

<table>
<thead>
<tr>
<th>Graft delivery</th>
<th>Clinical course</th>
<th>POP (μm) 6 mo/ red. %</th>
<th>BSCVA at 6 months</th>
<th>Graft ECD in cells/ mm²</th>
<th>Δ ECD 6 mo</th>
<th>Eventual status and remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICL injector cartridge</td>
<td>Good</td>
<td>504 / 19.5%</td>
<td>0.7 (20/30)</td>
<td>2500</td>
<td>70.6%</td>
<td>Clear transplant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(736)</td>
<td>Minimal partial peripheral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>detachment</td>
</tr>
<tr>
<td>ICL injector cartridge</td>
<td>Complete</td>
<td>1026 / -2.8%</td>
<td>0.001</td>
<td>n.a.</td>
<td>n.a.</td>
<td>Regrafted at 6 months</td>
</tr>
<tr>
<td></td>
<td>detachment at 1.5 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICL injector cartridge</td>
<td>Good</td>
<td>537 / 24.9%</td>
<td>1.0</td>
<td>2500</td>
<td>77.2%</td>
<td>Clear transplant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(571)</td>
<td>Paracentral folds</td>
</tr>
<tr>
<td>ICL injector cartridge</td>
<td>Good</td>
<td>659 / 3.4%</td>
<td>0.5</td>
<td>2000</td>
<td>n.a.</td>
<td>Initially clear transplant,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>late failure. Regrafted at 9 months</td>
</tr>
<tr>
<td>ICL injector cartridge</td>
<td>Good</td>
<td>509 / 20.5%</td>
<td>0.4</td>
<td>2667</td>
<td>78.6%</td>
<td>Clear transplant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(570)</td>
<td>Low visual potential (macular hole)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial partial detachment at 1° week, fully attached after rebubbling.</td>
</tr>
<tr>
<td>ICL injector cartridge. Femto-second DMhexis</td>
<td>Good</td>
<td>497 / 21.2%</td>
<td>1.0</td>
<td>3344</td>
<td>29.7%</td>
<td>Clear transplant, minimal fold</td>
</tr>
<tr>
<td>ICL injector cartridge</td>
<td>Good</td>
<td>449 / 22.5%</td>
<td>0.8</td>
<td>2525</td>
<td>24.2%</td>
<td>Clear transplant</td>
</tr>
<tr>
<td>ICL injector cartridge. Femto-second DMhexis</td>
<td>Good</td>
<td>422 / 25.6%</td>
<td>1.0</td>
<td>2809</td>
<td>52.0%</td>
<td>Clear transplant</td>
</tr>
</tbody>
</table>

**AVG 0.8 ± 0.2**

75.0% (6/8) ≥ 0.5  
62.5% (5/8) ≥ 0.8  
37.5% (3/8) ≥ 1.0

55.4 ± 24.0%  
(1248.3 ± 755.0)

75% (6/8) Success  
25% (2/8) Regrafted  
No pupillary block glaucoma
Worth, USA). Using an implantable Collamer lens injector and cartridge (Staar; Nidau, Switzerland) filled with balanced saline solution (BSS), the grafts were encapsulated within two viscoelastic plugs (Provisc Plus, Alcon). The DM rolls were inserted into the anterior chamber and then oriented endothelial side down using careful indirect manipulation of the tissue with air and BSS. An x-shaped 10/0 nylon suture was used to seal the main incision. An air bubble was used to extend the graft and then re-injected underneath to position the tissue onto the recipient posterior stroma. The anterior chamber was completely filled with air for 60 minutes, followed by air-liquid exchange to pressurize the eye. A final 60% air bubble was left in the eye overnight.

Patients were placed on a regimen of 1% dexamethasone drops qid, tapered down over a period of six months to fluorometholonone bid.

Postoperatively, patients were evaluated at 1 day, 1 week, 4 weeks, and 1, 3 and 6 months after surgery. BSCVA, endothelial specular microscopy (Topcon SP3000; Tokyo, Japan) as well as slit lamp photography and Visante anterior segment OCT (Carl Zeiss Meditec; Henningsdorf, Germany) imaging data were recorded in a MySQL database.

**RESULTS**

The procedure was successful in all patients except for cases 2 and 4 (Table 1, Figure 5), which suffered a complete graft detachment and late failure. Both received a successful DMEK regraft afterwards. Overall success rate was 75% (6/8) at six months.

**Endothelial cell density**

At six months ECD data was available for eight patients. Mean ECD loss was 55.4 ± 24.0% with an absolute mean ECD of 1248.3 ± 755.0 cells/mm².

**Visual acuity**

Overall, at six months 75% (6/8) of patients had reached BSCVA ≥ 0.5, 62.5% (5/8) reached ≥ 0.8, and 37.5% (3/8) reached ≥ 1.0. Visual quality analysis on eyes with good visual potential excluded two cases which needed a secondary graft and one with macular hole; 100% (5/5) reached BSCVA ≥ 0.5, 80% (4/5) ≥ 0.8, and 60% (3/5) 1.0 (Figure 1).

**Complications**

Complete graft detachment occurred in 12.5% (1/8) of surgeries (case 2, table 1, Figure 5), while partial detachments were observed in 25% (2/8) of cases (cases 1 and 5 in figures 3 and 4, respectively). Re-bubbling was required in 12.5% (case 5) and has remained attached since. Paracentral folds were found in 12.5% (case 3 in figure 3) but did not affect vision. Twenty-five percent (25%) (2/8) required a regraft, due to complete detachment and late failure. No postoperative pupillary block glaucomas or acute primary graft failures (fully attached graft which fails to clear) were recorded.

**DISCUSSION**

Since the clinical onset of Fuchs’ dystrophy typically occurs in elderly patients, there is a high prevalence of concomitant cataract, which often poses a dilemma about the timing of the lens extraction. Several authors have described the combined triple DSAEK and phacoemulsification procedure, and have reported the advantages over two-stage procedures. In a series of 200 DSAEK procedures, Terry et al. reported having combined 103 of those (52%) with phacoemulsification immediately prior to the endothelial replacement, and affirmed the advantages of using cohesive viscoelastics such as Healon (Advanced Medical Optics; Santa Ana, CA, USA) to lift the donor and prevent later detachment.

In contrast, DMEK, being a relatively new technique, is still not routinely performed with simultaneous cataract surgery. Dapena et al. first described the survivability of DMEK grafts after cataract surgery in a patient who had been previously grafted six months earlier and attained visual acuity of 1.0 and ECD of 1,019 cells/mm² three months after cataract extraction. Along the same line, Ham et al. have advocated cataract extraction before commencing DMEK, firstly, because 10% to 30% of eyes are likely to achieve satisfactory visual acuity after cataract extraction, allowing postponement of transplantation, and secondly, because of concerns that viscoelastic during the procedure may lead to an increased graft detachment rate. Furthermore, other groups have reported the use of cohesive viscoelastic in phacoemulsification and DSAEK to be effective for reattaching dislocated grafts in abnormally...
In the first prospective study on DMEK in the United States, Price et al. successfully combined ten DMEK with phacoemulsification and IOL implantation as a triple procedure to treat coexisting cataract and Fuchs' endothelial dystrophy\textsuperscript{12}. Later, Guerra et al. reported a larger series of 136 eyes, in which 23 were approached with the same triple procedure\textsuperscript{13}. Recently, Laaser et al. published a retrospective study in which 61 eyes were treated with the new DMEK "advanced triple procedure", without a significant increase in cell loss, detachments or complications\textsuperscript{14}.

In our current study, we explored the feasibility of combining DMEK with our standard cataract surgery. Our eight operated eyes had in common a disease onset around the sixth decade of life, advanced-stage cataract, corneal edema due to advanced endothelial disease with significant corneal edema and bullae, and shallow anterior chambers (mean ACD 2.4 ± 0.5mm). The rationale behind our approach was to consider three surgical options: First, lens extraction followed by DMEK some time later; second, DMEK followed by lens extraction some time later; third, lens extraction and simultaneous combined DMEK in the same procedure (DMEK alone was not considered since patients were significantly limited by their cataract). It was considered that the first option would be impossible because the corneal visibility would have rapidly deteriorated within a short time, thus rendering the subsequent surgery very difficult. The second option would also be technically difficult because a very shallow anterior chamber would hamper unfolding of the graft. Finally, we hypothesized that the third option would be more feasible by first removing the bulk of the cataract, stabilizing the posterior chamber with an in-the-bag IOL, and immediately afterwards performing the DMEK in an enlarged anterior chamber. A further advantage would be the need for one single procedure to solve both problems. It was unclear whether viscoelastics would induce higher graft detachment, and whether phacoemulsification-induced inflammation could affect the graft.

After the combined procedure, seven of the eight patients showed long term corneal transparency, and all improved in terms of BSCVA and central pachymetry. As planned, all patients had an increased postoperative ACD due to the cataract extraction. The best visual acuity corresponds to cases 3, 7, and 9 (table 1, figure 7), reaching 1.0. In contrast, case number 2 developed an insidious complete

**Perioperative**

**6 Months postoperative**

Figure 2. Collage of slit lamp images, Visante as-OCT pachymetry and tomography before surgery, one day after surgery (slit lamp) and 6 months after surgery (slit lamp, Visante). Cases 1 (top) and 6 (bottom).
graft detachment, confirmed one month after surgery by Visante OCT examination; this was later successfully regrafted. In case 8, a subclinical rejection cannot be ruled out since cell loss was acceptable at six months but decreased afterwards. The regraft was also successful. Case 5 had a partial detachment and needed re-bubbling the first week. The graft has remained attached and clear since, but showed long term mild peripheral scarring in the stromal-graft interface (figure 6). Case 1 had a minimal peripheral fold which required no treatment (figure 4).

Our results show a promising success rate of 71.4% clear corneas at six months, without any primary graft failures, understood as a fully attached graft which fails to clear. Our results correlate well with those of the initial learning curve for DMEK reported by Dapena et al.7

BSCVA, ACD and central pachymetry did improve in

Figure 3. Slit lamp image of case 3 showing paracentral folds (arrows) six months after surgery.

Figure 4. Slit lamp image and as-OCT Visante of case 1 showing an initial peripheral fold (arrows) at 1 month after surgery. No treatment was required.

Figure 5. Slit lamp image and as-OCT Visante of case 2 showing a complete graft detachment 4 months after surgery.

Figure 6. Slit lamp image and as-OCT Visante of case 5 showing a partial detachment 15 days postoperatively (left, arrow) and later full attachment by re-bubbling. Late thickening of the DM-stromal interface (right, arrow) at 6 months after surgery.
all functioning grafts; 100% reached 0.5 or better and 66.8% 0.8 or better at six months. Complete detachment was about 10% better in our series. On the other hand, endothelial cell survival is a greater concern because larger series have reported 34-39% loss, whereas our series seems to have lost 18% more.15,17 However, because an initial cell loss in the early months is usually followed by a long-term plateau, we expect our grafts to remain clear for much longer.18,19 Further observation of our patients will answer concerns on the long-term survival of these grafts.

The success of our procedure in terms of attachment stability was probably due to conservative use of ultrasound parameters in the phacoemulsification system, use of a cohesive viscoelastic only, and its complete and methodic removal. With more experience, femtosecond laser may prove to be a useful tool for adding precision and predictability to the procedure. The choice of DMEK as theEK technique to combine in a triple procedure seems to be more advantageous than the same procedure using PK or DSAEK because of faster visual rehabilitation, better graft adherence and avoidance of an open-globe situation. A future, prospective comparative randomized study may further validate this approach.

REFERENCES