ABSTRACT

Purpose: To report the two-year results of Descemet membrane endothelial keratoplasty (DMEK) for managing corneal endothelial disorders.

Methods: Non-randomized prospective clinical trial. A DMEK was performed in ten patients with Fuchs’ endothelial dystrophy or bullous keratopathy. A 3.5 mm clear corneal incision was made and «under air» DM was stripped off from the posterior stroma. A 9.0 mm diameter, organ cultured donor DM roll was inserted into a recipient anterior chamber, positioned into the posterior stroma and secured by completely filling the anterior chamber with air for 30 minutes.

Results: Three eyes showed complete detachment of the tissue; this was managed by a secondary Descemet stripping endothelial keratoplasty procedure. The remaining seven eyes had a best corrected visual acuity of ≥ 0.7 in three eyes (43%) at one month, in five eyes (71%) at six months, and in six eyes (86%) at one and two years. At six months, the endothelial cell density averaged 2039 (±373)

RESUMEN

Objetivo: Describir los resultados, dos años después de realizar una queratoplastia endotelial de membrana de Descemet (DMEK: Descemet membrane endothelial keratoplasty), para el tratamiento de alteraciones del endotelio corneal.

Métodos: Estudio clínico prospectivo no randomizado. En 10 pacientes con distrofia endotelial de Fuchs o queratopatía bullosa, se practicó una DMEK. A través de una incisión de 3,5 mm en córnea clara, la membrana de Descemet (MD) del receptor fue desprendida del estroma posterior en presencia de aire. Un disco de 9 mm de diámetro enrollado de MD donante preservada, fue insertado en la cámara anterior del receptor, posicionado en contacto con el estroma posterior corneal y asegurado en su posición mediante el llenado completo de la cámara anterior con aire durante 30 minutos.

Resultados: Tres ojos mostraron un desprendimiento completo del tejido donante, por lo que fueron sometidos posteriormente a una queratoplastia endotelial con «pelado» de la MD (DSEK: Desce-
INTRODUCTION

In recent years we have described several posterior lamellar keratoplasty procedures which allowed the substitution of the corneal endothelium without incisions or sutures in the corneal surface for managing Fuchs’ endothelial dystrophy and aphakic or pseudophakic bullous keratopathy. In 1998 we described a technique in which a 7.5 mm diameter posterior lamellar disc without sutures could be transplanted through a 9.0 mm scleral incision with posterior suture (1-3). Since 2001, this technique became known in the United States as Deep Lamellar Endothelial Keratoplasty (DLEK) (4). In 2000 we described a variant of the previous technique that does not require sutures, in which a disc-shaped posterior transplant with a diameter of 9.0-9.5 mm was inserted through a 5.0 mm self-sealing incision in the anterior chamber (5). Since 2005, this technique has become known in the United States as «small incision DLEK» (6). In 2003, we described the insertion of a donor posterior disc folded in combination with a «descemetorhesis» for removing the endothelial layer and its Descemet Membrane (DM) from the receptor (7,8). At present, this technique is known as Descemet’s stripping endothelial keratoplasty: DSEK) (9,10).

Even though the above techniques, designed and developed by our institute, demonstrated their feasibility for transplanting a donor posterior corneal disc without sutures, it could be expected that the selective DM and endothelium transplant would provide the best possible recovery of visual capacity in a corner with endothelial alteration (11-15). This study describes the clinical results after two years of an isolated DM transplant through a 3.5 mm self-sealing incision in a clear cornea, which could be termed «Descemet Membrane Endothelial Keratoplasty» (DMEK) (13-15).

SUBJECTS, MATERIAL AND METHODS

The DMEK was performed in four males and five females from 45 to 87 years of age with Fuchs’ endothelial dystrophy and/or bullous keratopathy (table I). All the patients signed an informed consent approved by the Institutional Review Board (IRB).

Donor tissue

In 10 donor ocular globes having less than 36 hours post mortem the corneal-scleral rings were...
extracted and stored in a minimally modified essential medium (MMEM) at 31°C for organ culture. The mean age of donors was 71.3 years (SD: 6.1) and the mean cellular endothelial count of the tissue was 2614 (SD: 186) cel/mm² (Table).

After two weeks in culture medium without dextran and with antibiotics at 31 °C the morphology and feasibility of the endothelial cells was assessed by means of inverted microscopy (Axiovert 40. Zeiss, Göttingen, Germany). Subsequently the corneal-scleral rings were assembled with the endothelial surface upwards upon a custom-designed vacuum holding instrument and the DM was detached from the posterior stroma using thin tweezers to obtain a 9.0 mm diameter endothelial single layer of DM. Due to the elastic properties of Descemet’s membrane it rolled up spontaneously to form what is known as a «Descemet-roll», with the endothelium facing outwards. Each «Descemet-roll» was subsequently stored in a dextran-free organ culture medium with antibiotics for a maximum period of one week awaiting transplant.

### Table I. Descemet Membrane Endothelial Keratoplasty (DMEK): 2-year results

<table>
<thead>
<tr>
<th>#</th>
<th>Age (years)</th>
<th>Sex</th>
<th>RE/LE</th>
<th>Surgery indication</th>
<th>Pre-surgery</th>
<th>Donor</th>
<th>Surgery</th>
<th>Post-surgery</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>M</td>
<td>LE</td>
<td>FED (pseudophakic)</td>
<td>None</td>
<td>0.3</td>
<td>2960</td>
<td>No</td>
<td>1.0 1.25 1.0</td>
</tr>
<tr>
<td>2</td>
<td>61</td>
<td>F</td>
<td>RE</td>
<td>PPBK</td>
<td>None</td>
<td>FC</td>
<td>2630</td>
<td>Complicated graft insertion</td>
<td>n.r. n.r. n.r.</td>
</tr>
<tr>
<td>3</td>
<td>87</td>
<td>F</td>
<td>LE</td>
<td>PPBK</td>
<td>Pupil fixed and RPE changes after complicated phako</td>
<td>0.1</td>
<td>2460</td>
<td>No</td>
<td>0.25 0.4 0.4</td>
</tr>
<tr>
<td>4</td>
<td>86</td>
<td>F</td>
<td>RE</td>
<td>FED (pseudophakic)</td>
<td>Superficial stromal scar</td>
<td>0.3</td>
<td>2640</td>
<td>Vitreous pressure</td>
<td>n.r. n.r. n.r.</td>
</tr>
<tr>
<td>5</td>
<td>72</td>
<td>M</td>
<td>RE</td>
<td>FED (pseudophakic)</td>
<td>Sub-epitelial central corneal scar</td>
<td>0.1</td>
<td>2660</td>
<td>Exenteric donor pressure</td>
<td>0.5 0.6 0.7 0.7</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>M</td>
<td>LE</td>
<td>FED (pseudophakic)</td>
<td>None</td>
<td>0.3</td>
<td>2470</td>
<td>No</td>
<td>1.0 1.0 1.0 1.0</td>
</tr>
<tr>
<td>7</td>
<td>76</td>
<td>F</td>
<td>LE</td>
<td>FED (pseudophakic)</td>
<td>None</td>
<td>0.3</td>
<td>2520</td>
<td>No</td>
<td>0.6 0.8 1.0 0.9</td>
</tr>
<tr>
<td>8</td>
<td>59</td>
<td>M</td>
<td>RE</td>
<td>BK eci (phakic)</td>
<td>None</td>
<td>0.8</td>
<td>2480</td>
<td>No</td>
<td>1.0 1.0 1.0 1.0</td>
</tr>
<tr>
<td>9</td>
<td>74</td>
<td>F</td>
<td>LE</td>
<td>FED (pseudophakic)</td>
<td>None</td>
<td>0.3</td>
<td>2640</td>
<td>No</td>
<td>0.6 0.7 0.8 1.0</td>
</tr>
<tr>
<td>10</td>
<td>45</td>
<td>F</td>
<td>RE</td>
<td>FED (phakic)</td>
<td>SEL</td>
<td>0.5</td>
<td>2640</td>
<td>Incomplete donor division</td>
<td>n.r. n.r. n.r. n.r.</td>
</tr>
</tbody>
</table>

### ARMD = Age-Related Macular Degeneration; DSEK = Descemet stripping endothelial keratoplasty; FC = Finger Counting; n.r. = Not relevant; BCVA = Best Corrected Visual Acuity (Snellen); ECD = Endothelial Cell Density; PPBK = Pseudo-Phakic Bullous Keratopathy; SEL = Systemic Erythematous Lupus; MD = Descemet Membrane; FED = Fuchs Endothelial Dystrophy; RPE = Retinal Pigmentary Epithelium; BMC = Biomicroscopy; BK eci = Bullous Keratopathy of unknown origin; m = Months; n.a. = Not available.

### Surgery

An epithelial mark having a diameter of 9.0 mm was made in the recipient eyes to circumscribe the DM excision area. A 3.5 mm tunnelized incision was made in the limbus, penetrating the anterior chamber exactly at the limit of said mark. Utilizing a custom-made scraper (Melles scraper, D. O. R. C. International, Zuidland, The Netherlands) a circular portion of DM was removed from the posterior stroma in the presence of air, carrying out a «descemetorrhexis» of 9.0 mm diameter and removing from the eye the central portion thereof (7,8).

The donor «Descemet-roll» was dyed with a 0.06% trypan blue solution (VisionBlue™, D. O.
R. C. International) and inserted in a custom-made injector (Hippocratesch, Rotterdam, The Netherlands) (11,12). Utilizing the injector, the donor «Descemet-roll» was inserted in the anterior chamber and carefully extended over the surface of the iris by indirect manipulation of the tissue with air and a balanced saline solution. Subsequently, an air bubble was injected under the donor DM to position it and maintain the tissue in contact with the recipient posterior stroma (11,12). The anterior chamber was completely filled with air for 30 minutes followed by an air-liquid replacement for pressurizing the eye.

**Endothelial assessment**

The cellular feasibility of the donor endothelial was assessed by means of inverted light microscopy (Axiovert 40. Zeiss, Göttingen, Germany), taking digital photographs (PixelINK LP-A662, Zeiss, Göttingen, Germany) after administering 1.8% sucrose and dyeing with 0.04% blue tryphan (15-17). The endothelium of the patients was photographed and assessed utilizing a non-contact autofocus Topcon SP3000p mirror microscope (Topcon Corp, Tokyo, Japan). The images of the central cornea were manually analyzed and corrected, averaging three measurements of the endothelial cellular density (15-17,19,20).

**RESULTS**

The first day post-op all the donor DMs exhibited full adhesion to the posterior stroma of the receptor. One week after the operation, the Descemet transplant retained its position in seven of the eyes, but the three remaining eyes (cases 2, 4 and 10) exhibited a complete detachment of the donor membrane, with the graft appearing rolled up and floating in the anterior chamber. In these eyes a DSEK was performed without complications two or three weeks after the initial DMEK surgery.

In the seven eyes that exhibited complete adhesion of the graft we observed a best corrected visual acuity (BCVA) <0.7 in three eyes (43%) one month after surgery, in five eyes (71%) six months after surgery and in six eyes (86%) within the first and second year (table I). At six months after surgery, the mean endothelial cell density was of 2039 (SD: 373) cell/mm² (n=7) and at the first and second year of 1925 (SD: 267) cell/mm² (n=7) and 1730 (SD: 400) cell/mm² respectively (fig. 1, Table I).

Initially, it was difficult to visualize the transplant in the receiving eye. The confirmation that the transplant was in the right position was obtained observing its contour which showed a reflecting brilliance on the donor DM and by means of mirror microscopy which identified the paracentral endothelial donor cells. Some eyes exhibited small peripheral DM «tags», indicating the presence of DM micro-detachments or folds in the external limit of the transplant. With time, these peripheral tags stabilized and did not increase in size.

**DISCUSSION**

In 1998 we described that the DM transplant was technically possible in a cadaver human eye model (11,12). At the time, obtaining a DM from a donor corneal-scleral ring was seen as a challenge without the support of an eye bank. As on some occasions the peeling of the DM could be a challenge due to the inadvertent tearing of the membrane, the donor DM should preferably be prepared in the eye bank prior to surgery instead of during the operation itself. When the Amnitrans Eye Bank was established in Rotterdam (Amnitrans Eyebank Rotterdam) in January 2004, all its facilities and logistics were available for routine preparation of Descemet’s membrane transplants, and the assessment of its endothelial cell layer and the microbiological study of the tissue to ensure its sterility. Since then, extensive lab studies were made to simplify the procedure (14-18). In addition, a number of technical modifications were designed for the surgical implantation of the donor DM layer, its manipulation in the anterior chamber and its full adherence to the receiving posterior stroma. (Melles CRJ, unpublished data, 2005) (14,15).

Recently, the possibility of transplanting an isolated DM was also demonstrated by Tappin and Pavel utilizing different approaches. Tappin designed an instrument for inserting a 7.5 mm diameter donor DM in the anterior chamber through a sutured 8.0 mm incision (21). Pavel described the DM donor tissue transplant linked to a stromal peripheral ring to facilitate its handling (P. Studeny. Descemet's membrane with stromal hem transplantation. Winter ESCRS 2007). In this study, we transplanted...
DM with endothelium through a small tunnelized incision as previously described (11,12). Taking into account the terms utilized for differentiating different posterior lamellar keratoplasty procedures, the instant procedure, i.e. the isolated donor DM transplant carrying a feasible endothelial cell layer, was initially termed DMEK.

The challenge in designing any posterior lamellar keratoplasty procedure is to provide a sufficiently high endothelial cellular density to obtain a long-term survival of the graft. In this study, both objective and subjective measures indicated that DMEK could be potentially able to achieve cellular densities approaching 2000 cells/mm² in the mid-term, comparable to those obtained after DLEK and DSEK (6-19).

In comparison with the posterior lamellar keratoplasty techniques we designed in the past such as DLEK and DSEK (14), DMEK could have five main advantages: Firstly, this study suggests that the visual recovery after DMEK could be much faster than after DLEK or DSEK because six out of seven eyes with DMEK achieved a BCVA ≥ 0.5 one month after surgery (table I). In addition, in the first series described of 50 patients submitted to DMEK due to Fuchs’ endothelial dystrophy, 95% exhibited a BCVA ≥ 0.50.5, and more importantly 75% achieved a BCVA ≥ 0.8 six months after surgery (22). These numbers are in contrast with DLEK or DSEK procedures which have demonstrated a mean BCVA ≥ 0.5 in an average time of six or more months (6,9,23). The difference in the visual acuity recovery might suggest that the presence of donor posterior stroma in DLEK and DSEK is what primarily determines the degree of visual recovery instead of secondary changes or edema in the receiving corneal stroma, because in DMEK there is no transplanted donor posterior stroma.

However, in order to perform a DMEK it is necessary to have an adequate visualization of the anterior chamber due to the greater surgical complexity of the procedure. Therefore, in severely unbalanced corneas, in the presence of training devices for glaucoma, narrow anterior chamber or low potential for visual rehabilitation, it would be recommendable to perform a DSEK which is technically less challenging.

In second place, as DMEK could provide a near-perfect restoration of the corneal anatomy and a better quality of the cornea, with this technique we could expect a greater recovery of the visual capacity (11,12). Accordingly, in DMEK the end visual

---

**Fig. 1:** Slit lamp photograph of a transplanted cornea one year after performing DMEK (Case 6). A) notice the transparency of the transplanted cornea and the invisible anatomic interphase between the donor and host tissue. B) Notice the periphery of Descemet’s membrane signaled by the yellow arrow.
result might be limited only by the quality of the anterior portion of the receiving cornea prior to surgery.

In Fuchs’ endothelial dystrophy it is not rare for visual acuity to be unrelated to the visual symptoms of the patient, and therefore in these cases VA would not be a good indicator for surgery. An example is case number 8 that exhibited a BCVA of 0.8 but a significantly decompensated cornea with sub-epithelial secondary changes and a significant alteration of sensitivity to contrast and color perception.

In the third place, in DMEK the diameter of the graft can be of 9.0 up to 11.0 mm, which means that a greater endothelial cell surface is transplanted compared to DLEK (7.5 to 8.0 mm) or DSEK (8.5 to 9.5 mm). In our experience, even though the correlation between the diameter of the graft and its survival has not been demonstrated, we could expect that a larger graft in DMEK will benefit the long-term survival of the transplant.

Fourth, DMEK could demonstrate a better fulfillment of current requirements for anterior segment of modern surgery because the donor DM can be transplanted through a tunnelized incision in a clear cornea, which is widely utilized in phacoemulsification surgery and is known to induce a minimum post-op astigmatism (17,24,25). Even though several instruments have been described for inserting a donor DM (21,26,27), its utilization could Limit the end diameter of the graft (6.0 to 7.5 mm), in addition to requiring a relatively large entry incision.

Fifth, in contrast with DLEK and DSEK, where the majority of surgeons would require a microkeratome or femtosecond laser, in DMEK the donor DM films can be «peeled» directly from a corneal-scleral ring. With our technique for preparing 9.0 mm DM films from concave donor corneal-scleral rings, the magnitude of the cellular lesion expressed in the «percentage of damaged mean endothelial surface area» is of 3.4% (11,12,18). Similar results were found by Ignacio et al, who obtained Descemet transplants from convex rings (28), and Zhu et al, who preserved rectangular films from concave rings (29). It is important to emphasize that all of the studies were made in preserved tissue, either in cold storage or in organ culture medium. Accordingly, if it is possible to routinely obtain viable grafts from preserve tissue, DMEK could be much more accessible for the majority of corneal surgeons than DLEK or DSEK.

As with DSEK/DSAEK, the graft detachment was the most frequent complication in DMEK. In the first described series of 50 patients submitted to DMEK due to Fuchs’ endothelial dystrophy, the rate of detachment was 25%. However, when analyzing the last 25 patients who were intervened with this procedure, the detachment rate went down to 12%. This reduction was related to the learning curve, changes in the surgical technique and in the techniques utilized in the eye bank as well as to the extension of the time for filling the anterior chamber with air in 45-60 minutes (22). In our experience, the most important factor for obtaining a complete adhesion of the donor tissue is to avoid the use of hyaluronic acid throughout the procedure (14). As with DSEK, all viscoelastics should be avoided in DMEK because the detachment of the donor tissue is strongly correlated with their utilization (14). In vitro experiments have proved that filling the anterior chamber with air for at least 30 minutes is essential to obtain a complete adhesion of the donor tissue in DMEK whereas an air filling of only 15 minutes would be sufficient in DLEK and DSEK (8,14).

Our experience with DMEK suggests that the transplant of isolated donor DM carrying feasible endothelium for treating alterations of the corneal endothelium provides a near-perfect anatomic restoration and a high degree of visual rehabilitation. As in DLEK and DSEK, the main drawback of the procedure is the risk of detachment of the graft in the early post-op (16). When the percentage of detachments in DMEK can be reduced due to improvements in the eye bank logistics and also in the surgical technique, the project of posterior lamellar keratoplasty should finally be completed.

REFERENCES