Original article

Visual acuity and endothelial cell density following Descemet membrane endothelial keratoplasty (DMEK)

I. Dapena\textsuperscript{a,f,g,h,*}, L. Dapena\textsuperscript{b,c}, M. Dirisamer\textsuperscript{a,f,g,h}, L. Ham\textsuperscript{d,f,g,h}, G.R.J. Melles\textsuperscript{a,e,f,g,h,*}

\textsuperscript{a} Graduate in Medicine
\textsuperscript{b} Graduate in Veterinary Sciences
\textsuperscript{c} Ph.D. University of León
\textsuperscript{d} Graduate in Health Sciences
\textsuperscript{e} Ph.D. in Medicine
\textsuperscript{f} Netherlands Institute for Innovative Ocular Surgery, Rotterdam, Netherlands
\textsuperscript{g} Melles Cornea Clinic Rotterdam, Rotterdam, Netherlands
\textsuperscript{h} Amnitrans EyeBank Rotterdam, Rotterdam, Netherlands

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\textbf{Abstract}

Purpose: To assess the clinical outcomes of DMEK in the first series of 120 eyes operated for the treatment of Fuchs endothelial dystrophy in terms of visual acuity and endothelial cell density.

Methods: The first 120 consecutive eyes that underwent DMEK (i.e. transplantation of an isolated donor Descemet membrane with its endothelium) were evaluated. In all eyes, the best corrected visual acuity (BCVA) before and at 1, 3 and 6 months after surgery, as well as the endothelial cell density (ECD) before and at 6 months were measured.

Results: In eyes with a functional DMEK graft and good visual potential (n = 96), the BCVA was $\geq 20/40$ ($\geq 0.5$) in 77% after 1 month, 92% after 3 months, and 95% after six months; $\geq 20/25$ ($\geq 0.8$) in 50%, 63%, and 73% of the cases, and $\geq 20/20$ ($\geq 1.0$) in 23%, 34%, and 45% of the cases at 1, 3, and 6 months, respectively. In this group, ECD averaged 2610 ($\pm 185$) cells/mm$^2$ before, and 1770 ($\pm 520$) cells/mm$^2$ at six months after surgery (n = 96). In 15 eyes, a secondary Descemet stripping endothelial keratoplasty (DSEK) was performed. In this group, 91% of patients reached a BCVA of $\geq 20/40$ ($\geq 0.5$) and only one patient achieved a BCVA of 0.8 at 6 months after surgery (n = 11). Furthermore, ECD averaged 2580 ($\pm 185$) cells/mm$^2$ before and 1310 ($\pm 740$) cells/mm$^2$ at six months (n = 13).

Conclusion: DMEK provides a fast and high visual rehabilitation. Endothelial cell density loss may be similar to earlier types of endothelial keratoplasty.

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* Corresponding authors.
E-mail addresses: isadapena@gmail.com (I. Dapena), melles@niioc.nl (G.R.J. Melles).
Agudeza visual y densidad de células endoteliales tras queratoplastia endotelial de membrana de Descemet (DMEK)

RESUMEN

Objetivo: Evaluación de los resultados visuales y de la densidad de células endoteliales en los 120 primeros ojos sometidos a queratoplastia endotelial de membrana de Descemet (DMEK) como tratamiento para la distrofia endotelial de Fuchs.

Material y métodos: Se evaluaron los primeros 120 ojos sometidos a DMEK. En todos ellos se midió la agudeza visual mejor corregida (AVMC) antes y al 1, 3 y 6 meses después de la cirugía, así como la densidad celular endotelial (DCE) antes y a los 6 meses.

Resultados: En los ojos con transplante exitoso y sin patologías concomitantes (n = 96), se observó una AVMC ≥ 0,5 en el 77% de los casos al mes de la cirugía, en el 92% a los 3 meses y en el 95% a los 6 meses. La AVMC fue ≥ 0,8 en el 50%, 63% y 73% de los casos y ≥ 1,0 en el 23%, 34% y 45% al 1, 3 y 6 meses después de la cirugía, respectivamente. La DCE preoperatoria fue 2.610 (± 185) células/mm² y 1.770 (± 520) células/mm² a los 6 meses postcirugía. En quince ojos se realizó una queratoplastia endotelial con pelado de la membrana de Descemet (DSEK) secundaria. En este grupo, el 91% de los pacientes alcanzó una AVMC ≥ 0,5, alcanzando solo uno de ellos una AVMC de 0,8 (n = 11) a los 6 meses. Además, la AVMC media fue de 2.580 (± 185) células/mm² antes y de 1.310 (± 740) células/mm² a los 6 meses de la operación (n = 13).

Conclusiones: DMEK permite una rápida y casi completa rehabilitación visual. La DCE postoperatoria observada es comparable al obtenido con técnicas precedentes de queratoplastia endotelial.

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Introduction

In 1998, we described a first endothelial keratoplasty technique for treating corneal endothelium pathologies in which the altered layers were substituted by a posterior corneal layer (a posterior stroma layer with Descemet’s membrane and endothelium). This technique is now known as Deep lamellar endothelial keratoplasty (DLEK). A subsequent development of endothelial keratoplasty involved the introduction of “descemethorexis”, in which Descemet’s membrane with its endothelium was separated from the receiving cornea. In this way, the donor layer was placed in contact with the intact receiving stroma. This technique was denominated Descemet stripping (automated) endothelial keratoplasty (DSEK/DSAEK).

DLEK and DSEK/DSAEK were accepted widely because they reduced the typical complications of penetrating keratoplasty such as high astigmatism, suture-derived complications or incision dehiscence. Even though the visual results of the DLEK and DSEK/DSAEK techniques were better than for penetrating keratoplasty because they achieved a visual acuity of 0.5–0.6 after about 6 months post-surgery, they did not enable the maximum visual potential. The cause of this limited visual result could be because the excess stroma of the donor layer caused a distortion of the normal corneal anatomy. Under the assumption that the recovery of the normal corneal anatomy enhanced its optical quality and therefore improved vision, we have developed a modification of endothelial keratoplasty by means of, after “descemethorexis”, only the isolated Descemet membrane with endothelium is transplanted, excluding the stroma. We have called this technique Descemet membrane endothelial keratoplasty (DMEK).

As DMEK involves a greater surgical challenge, it should also provide better visual results for it to become a true development of the previous techniques. Accordingly, the purpose of this study is to analyze the results of the DMEK surgical technique for treating Fuchs endothelial dystrophy in terms of visual acuity and endothelial cell count.

Subjects, material and methods

Patients

This study comprised 120 DMEK-type operations, 105 patients, 46 males and 59 females with ages between 41 and 89 years (mean age 67.4 ± 12.4 years) who suffered Fuchs endothelial dystrophy (Fig. 1). Nineteen eyes were affected and the rest pseudophakic.

All the patients signed an informed consent approved by the Institutional Review Board (IRB).

Donor tissue

The corneas were obtained from donor ocular globes less than 36 h post-mortem. The corneal–scleral rings were removed and kept in organ culture tissue (CorneaMax, Laboratoires Eurobio, Les Ulis Cedex, France) at 31 °C. One week later, endothelial cell count was made (at least 2300 cells/mm²) and the morphology was analyzed.

For subsequent tissue preparation, the cornea was attached to a custom-design vacuum support and Descemet’s membrane (DM) was “peeled” off the posterior stroma utilizing small tweeters. Due to the elastic properties of DM, it rolled up spontaneously with the endothelium on the outer side.
The Descemet-roll was stored in organ culture medium during 5–10 days up to surgery time (Fig. 2).  

Surgical technique

All the interventions were made with retrobulbar local anesthesia. In the position at 12 o’clock from the limbus a 3.0 mm tunnelized, self-sealable incision was made, penetrating the anterior chamber. In order to have a better view of DM, the anterior chamber was completely filled with air and a 9.5 mm “descemethorexis” was performed through 2 paracentesis which enabled the DM to be detached and separated from the posterior stroma by means of Sinskey-type inverted hook (catalog number 50.1971B, D.O.R.C. International, Zuidland, Holland), extract in the central portion thereof. Subsequently it was verified that the DM had been completely dissected.  

The obtained Descemet “roll” was stained with 0.06% triphan blue (VisionBlue™, D.O.R.C. International) and aspirated in a custom-designed injector (Fa. Hippocratech, Rotterdam, Holland). It was inserted in the anterior chamber through the tunnelized incision and, by means of delicate maneuvers with air and a balanced saline solution (BSS), the graft was unrolled over the iris surface. Subsequently a bubble of air was injected below the donor Descemet’s membrane to place it in its final position and maintain the tissue in contact with the receiving posterior stroma. The anterior chamber was completely filled with air during 45–60 min, followed by an exchange of air-BSS in order to pressurize the eye, maintaining thereafter 50% of air filling in the anterior chamber.

Parameters of the study

All patients were assessed before and after surgery at 1, 3 and 6 months with biomicroscopy, Pentacam (Oculus, Wetzlar, Germany), and slit lamp photograph (Topcon Medical Europe BV).

The endothelial cell density (ECD) was determined in vitro (Axiovert 40 inverted light microscope, Zeiss, Göttingen, Germany), and photographed (PixiLINK PL-A662. Zeiss, Göttingen, Germany). In the patients, the ECD was assessed in vivo with non-contact mirror microscopy (Topcon SP3000p, Topcon Medical Europe BV, Capelle a/d IJssel, the Netherlands). The endothelial images corresponding to the central corneal were manually corrected, taking the value from the mean of 3 measurements.

The best corrected visual acuity (BCVA), ECD and intra- and post-surgery complications were collected in a database (MySQL database) and subsequently analyzed with the SPSS software (version 17.0. SPSS, Inc.).

Results

This study presents the analysis of the results of the first 120 DMEK-type surgeries performed in patients with Fuchs endothelial dystrophy. Of the 120 cases submitted to DMEK surgery (Table 1), in 15 eyes a secondary DSEK was performed without complications, while in 12 eyes and due to a total or partial graft detachment and in a further 3 due to primary transplant failure. Four eyes exhibited transplant detachment but, as the cornea cleared spontaneously, a second transplant was not required.

Nine eyes had a reduced vision prognosis due to other concomitant pathologies other than Fuchs endothelial dystrophy (one case of myopia Magnus, one case of amblyopia, 2 cases of retina detachment and 5 cases of macular alterations). All of these cases obtained a BCVA of ≤0.4 6 months after surgery.

Visual potential of DMEK

Of the 96 eyes with individual prognosis and successful DMEK, the presurgery BCVA was of ≤0.4 in 67/96 (70%) of patients and ≥0.5 in 29/96 (30%). However, 6 months after the surgery, 91/96 (95%) of patients achieved a BCVA of ≥0.5. 70/96 (73%), a BCVA of ≥0.8 and 43/96 (45%), a BCVA of ≥1.0 (Fig. 3 and Table 1). In addition, reduced mean pachymetry was observed between the presurgery value and the 6 months after surgery value, going from 670 μm (±97 μm) to 538 μm (±61 μm)

Fig. 1 – DSEK/DSAEK and DMEK techniques. Diagram showing procedures (A) DSEK/DSAEK and (B) DMEK. In both techniques, the receptor Descemet membrane is removed by means of “descemethorexis”. In DSEK/DSAEK, a posterior lamellar disc made up by posterior stroma, Descemet's membrane and its endothelium is transplanted, whereas in DMEK only an isolated Descemet membrane with endothelium and without stroma is transplanted.

Fig. 2 – Descemet graft in vial with culture medium. After peeling the Descemet’s membrane on the basis of a corneal–scleral ring from the eyes bank, the tissue spontaneously forms a “Descemet roll”.

A

DSEK / DSAEK

Donor

B

DMEK

Donor

Fig. 1 – DSEK/DSAEK and DMEK techniques. Diagram showing procedures (A) DSEK/DSAEK and (B) DMEK. In both techniques, the receptor Descemet membrane is removed by means of “descemethorexis”. In DSEK/DSAEK, a posterior lamellar disc made up by posterior stroma, Descemet's membrane and its endothelium is transplanted, whereas in DMEK only an isolated Descemet membrane with endothelium and without stroma is transplanted.
Table 1 – Exclusion criteria and results for DMEK at 1, 3 and 6 months.

<table>
<thead>
<tr>
<th></th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMEK: 120 eyes</td>
<td>BCVA (n = 96)</td>
<td>≥0.5</td>
<td>77%</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>≥0.8</td>
<td>50%</td>
<td>63%</td>
</tr>
<tr>
<td>15 eyes secondary DSEK (transplanted detachment or primary failure)</td>
<td>≥1.0</td>
<td>23%</td>
<td>34%</td>
</tr>
<tr>
<td>4 eyes detachment with Epithelial removal</td>
<td>Medium ECD (n = 96)</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
<tr>
<td>5 eyes limited visual prognostic (included for medium ECD)</td>
<td>ECD media (n = 13)</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
<tr>
<td>Secondary DSEK: 15 eyes</td>
<td>BCVA (n = 11)</td>
<td>≥0.5</td>
<td>18%</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>≥0.8</td>
<td>0%</td>
<td>9%</td>
</tr>
<tr>
<td>2 eyes limited visual prognostic (included for medium ECD)</td>
<td>≥1.0</td>
<td>0%</td>
<td>9%</td>
</tr>
<tr>
<td>2 eyes limited visual prognostic and endothelial cell count not available</td>
<td>ECD media (n = 13)</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
</tbody>
</table>

DMEK: Descemet membrane endothelial keratoplasty; DSEK: Descemet membrane endothelial keratoplasty with “peeling”; BCVA: best corrected visual acuity; ECD: endothelial cell density; n.r.: not relevant.

(n = 73), respectively. The donor tissue endothelial cell density prior to surgery was of 2610 (±185) cells/mm² and 1770 (±520) cells/mm² 6 months after surgery (n = 96) (Table 1).

The majority of eyes achieved adequate vision before 6 months, with a BCVA ≥0.5 in 74/96 (77%) of intervened eyes, one month after surgery and in 88/96 (92%) after 3 months. Visual acuity values ≥0.8 were observed after one month in 48/96 (50%) of intervened eyes and after 3 months in 60/96 (63%) and BCVA ≥1.0 was achieved in 22/96 (23%) and in 33/96 (34%) of eyes in the first and third month after surgery, respectively (Fig. 3 and Table 1).

In some cases, the recovery of the corneal anatomy was so positive that after surgery only small transplant details could be identified with the Slit lamp (Fig. 4) and the donor tissue could hardly be identified with anterior pole optic coherence tomography or with Scheimpflug tomograph (Fig. 5).

Spontaneous corneal clearing after DMEK

Four patients exhibited transplant detachment but with spontaneous corneal clearing and for the time being have not required a new transplant. All exhibited a preop. BCVA ≤0.4. Six months after surgery, one reached a BCVA of 0.8 and in the 3 remaining cases, BCVA was ≤0.4. The donor tissue ECD at month 6 was of 455 (±100) cells/mm² (n = 3).

Visual potential of DSEK as a “rescue” procedure

In 15 eyes a secondary DSEK was performed without complications. Four exhibited a reduced vision prognosis due to concomitant pathologies. In the 11 remaining eyes, BCVA before the surgery was ≤0.4 in 9/11 (82%) of patients and ≥0.5 in 2/11 (18%). Six months after the secondary DSEK, 10/11 (91%) achieved BCVA ≥0.5 with only one obtaining a BCVA of 0.8 (Table 1).

The presurgery endothelial cell density was of 2580 (±165) cells/mm² and 6 months after surgery it was of 1310 (±165) cells/mm² (n = 13) (Table 1).

Discussion

The analysis of the 120 first DMEK surgeries as a treatment for Fuchs endothelial dystrophy demonstrates that the Descemet membrane transplant is an efficient technique for eyes with only that pathology. With DMEK, visual acuities ≥0.5 are achieved in 95% of cases and ≥0.8 in 50% between 1 and 3 months after surgery, which constitutes an improvement when compared to other corneal transplant techniques.22,23

When comparing the results of DMEK with those obtained by previous endothelial transplant techniques such as DSEK/DASAEK, the new technique presents more favorable results. With DSEK/DASAEK, visual acuities of ≥0.5 are achieved in approximately 60% of cases, although not before 6 months after surgery, and visual acuities of ≥0.8 are achieved only in a few cases.14,24,25 If we compare the results with classic penetrating keratoplasty, in which only 40–50% achieved BCVA ≥0.5 after one year, DMEK would also provide better results.26

In order to evaluate the visual potential obtained with DMEK, we excluded from the study all eyes with concomitant ocular pathology or diseases with complicated developments (Table 1) (for example, bullous keratopathy secondary to cataract surgery complicated with edema macular). For this reason, this study included only eyes with Fuchs endothelial dystrophy.

In the light of the above results, the indications for performing the DMEK technique would be different than those for
DSEK/DSAEK or for penetrating keratoplasty. Accordingly, the advisability of awaiting for visual acuity to drop below 0.3 to perform endothelial transplant should be questioned because: in the first place, DMEK allows faster visual recovery and the final visual acuity would be obtained within 3 months after surgery. If DMEK does provide these positive results, similar to those provided by phacoemulsification for cataract surgery, then a higher pre-surgery visual acuity would be sufficient indication for carrying out the operation. Secondly, it must be taken into account that the visual acuity measurement is only one part of the subjective visual capacity. For instance, in 5 cases visual acuity did not change but even so patients described significant visual quality improvements. Therefore, the indication for a DMEK-type surgery would largely depend on the degree of involvement of the quality of life of the patient secondary to his/her corneal disease instead of age, visual acuity or endothelial count.

In case of cataracts associated to Fuchs endothelial dystrophy, it is recommendable to extract the cataracts prior to the DMEK instead of opting for combined surgery for the following reasons:

First, because 10–30% of eyes obtain sufficiently satisfactory visual acuity after cataract extraction and therefore the transplants could be deferred. Secondly, because cataract surgery requires the use of viscoelastic, a substance that seems to involve risks for transplant detachment in DMEK.2

In patients with Fuchs endothelial dystrophy and a relatively clear lens, it would be adequate to attempt to preserve the lens itself in order to maintain accommodation. In our series, despite the pharmacological miosis induced during

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**Fig. 4** – Slit lamp photograph of a cornea at month 1 (A) and month 6 (C) after performing a DMEK-type procedure, showing corneal transparency at month 1 after surgery while the interface between the donor and receptor tissue cannot be differentiated. (B and D) Mirror microscopy of the same cornea at month 1 and 6 after the intervention. The visual acuity was of 1.0 at month 1 post-DMEK.

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**Fig. 5** – Slit lamp photograph (A) and optic coherence tomography (B) of a cornea 12 months after DMEK. See how the donor Descemet’s membrane can be identified only by means of a small detachment (yellow arrow).
the operation, some affected patients exhibited slight anterior subcapsular lens opacity, possibly due to a lesion of the anterior capsule during the air buffering phase of the intervention.

The election of the most adequate surgical technique for treating Fuch's endothelial dystrophy would largely depend on corneal transparency because intra-surgery visualization of the transplant is necessary for the success of DMEK. Accordingly, DMEK would be indicated for treating Fuchs endothelial dystrophy in eyes with little corneal edema and good visual potential.

In eyes with complicated course, the Descemet 'roll' might be difficult to unroll and position adequately. In this case, the DSEK/DSEA technique would be more adequate.

In pseudophakic bullous keratopathy with large alterations in corneal transparency, it would be difficult to see the thin membrane utilized in the DMEK technique and, in eyes with a small angle with drainage valves for glaucoma, it could be technically difficult to unroll the Descemet transplant. In this situation, it would be recommendable to perform a surgery of the DSEK/DSEA type, in which the transplant consists in a thicker film and therefore it would be easier to identify and manipulate in the anterior chamber.

When comparing the complications of DMEK with those of DSEK/DSEA or of penetrating keratoplasty, due to the fact that the surgery is performed through a tunnelized incision of only 3 mm, there is lower refraction modification and therefore lower induced astigmatism, thus allowing the majority of patients to continue utilizing their usual spectacles until new ones are available. In addition and as with the previous DLEK and DSEK endothelial keratoplasty techniques, DMEK has the advantage that it does not require the use of contact lenses in the majority of older patients.1,2

As occurs with the DSEK/DSEA techniques, the main complication after a DMEK intervention would be transplant detachment in the early post-surgery phase. Initially, detachments were observed in 10–30% of cases, but after deciding to fill in the anterior chamber with air during 45–60 min the number of detachments diminished to 2–5%.17–19

In 2 cases, during the first day after surgery, intraocular pressure increased due to the migration of the air bubble behind the iris. By inducing pharmacological midriasis, the bubble returned to the anterior chamber which allowed the intraocular pressure to return to normal values.

In this group of 120 eyes submitted to DMEK interventions, a single episode of immunological rejection emerged 18 months after the transplant, which was resolved with topical corticosteroid treatment.

Although initially it was expected to have a large loss of endothelial cells after DMEK, the endothelial cell density was acceptable,27 with mean endothelial cell density reductions of 20–30% 6 months after surgery, which is an even lower reduction than the values produced by the DSEK/DSEA techniques.3,27

In this sense, it is not possible to make a statistical comparison but with a relatively high post-surgery cell count and the large size of the isolated Descemet transplant (9.5 mm) utilized in this study, transplant survival could be expected to be at least as good as that exhibited with the DSEK/DSEA technique. Some authors have suggested that the tissue transplants within the first week of donation would potentially reduce endothelial cell loss. However, this would hinder the previous preparation of the tissue in the eye bank, which would involve a significant disadvantage for many corneal surgeons who at present routinely receive "DM rolls" from the Rotterdam "Amnitrans Eyebank", thus avoiding the added concern of preparing the donor tissue the same day of the surgery.

In summary, the above results indicate that endothelial keratoplasty with the DMEK technique in patients with Fuchs endothelial dystrophy enables good vision within the first 3 months after surgery. As in the case of the DSEK/DSEA techniques, the main complication is transplant detachment in the early post-surgery period in 2–5% of cases.29

Conflict of interests

Dr. Melles is an advisor for D.O.R.C/Dutch Ophthalmic USA.

IRB/CI – the study was carried out in accordance with the requirements of the Institutional Review Board and of informed consent in accordance with the principles of the Helsinki declaration, in the Netherlands Institute for Innovative Ocular Surgery (study registration number N.N0.14). The study was submitted to http://www.clinicaltrials.gov (study registration number NCT00521898).

References