Complications after endothelial keratoplasty: three years of experience

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\textbf{Abstract}

\textbf{Objective:} To study the complications after Descemet's stripping automated endothelial keratoplasty (DSAEK).

\textbf{Methods:} Retrospective study of 75 eyes in 67 patients with Fuchs' endothelial dystrophy or bullous keratopathy operated on in the Instituto de Oftalmología La Arruzafa from March 2007 until March 2010. Phacoemulsification and IOL implantation was involved in 30 cases. All surgical and post-surgical complications, as well as the endothelial cell density were recorded.

\textbf{Results:} Graft detachment was the most common complication: 17 cases (22.5%); 16 of them resolved with reintroduction of air in the anterior chamber. The rate of detachment in cases without capsular support (8 eyes) increased up to 50%. Five cases had primary graft failure and, in 2 cases, a medium term failure was observed. Only one case of endothelial rejection was observed (1.3%). Five eyes (6.5%) developed a pupillary block, but of them were solved with the aspiration of the air. In one eye (1.3%), a posterior capsule rupture was observed during the phacoemulsification. This case ended with a retinal detachment. The endothelial cell loss was 42.75%.

\textbf{Conclusions:} DSAEK is an effective surgical technique to resolve the corneal edema due to endothelial failure; however, complications are not uncommon. Graft detachment is the most common complication, but is usually resolved with re-bubbling. There is an evident learning curve and the surgical trauma to the endothelium is the most important factor that influences the endothelial cell loss.

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Complicaciones tras queratoplastia endotelial: tres años de experiencia

\textbf{Resumen}

\textbf{Objetivo:} Examinar las complicaciones tras queratoplastia endotelial automatizada con disección de la membrana de Descemet (DSAEK).

\textbf{Palabras clave:} Queratoplastia
Distrofia de Fuchs


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Introduction

Automated endothelial keratoplasty with Descemet’s membrane stripping (DSEK: Descemet’s stripping with automated endothelial keratoplasty) is gaining popularity as the surgical treatment for corneal endothelial alterations, in contrast with penetrating keratoplasty (PK) due to the fact that the latter procedure is not free from drawbacks (prolonged visual rehabilitation, high astigmatism, complications related to stitching, infectious keratitis, incision dehiscence, endothelial rejection and even eventually expansive hemorrhages).1–4 In order to achieve a highly reproducible technique such as DSAEK, endothelial keratoplasty has evolved since in 1998 Gerrit Melles published the first successful case of corneal transparency restoration by changing the posterior corneal layers in a patient with bullous keratoplasty. A few years later, Mark Terry modified the instruments and began publishing important series of patients. Executing a descemetoectomy and obtaining a donor disc by means of a keratotomy performed with a microkeratome over an artificial anterior chamber has allowed the technique to be much more reproducible and both the donor and receiver substrates to be utilized in a more homogeneous manner. As this is a relatively new procedure, associated complications are still being described, with the donor graft dislocation being the most frequent one.5 In our center, DSAEK has been carried out 3 years ago. The objective of this paper is to illustrate the complications that have arisen and compare them with previously published studies.

Subjects, material and method

The clinical records of patients intervened from March 2007 to March 2010 with the DSAEK technique were retrospectively analyzed. In all cases, the surgical indication was due to a corneal edema caused by Fuchs’ endothelial dystrophy or bulous keratopathy. After surgery, the patients were assessed the following day, the third day, 1 week, 1 month, and after 3, 6, 12, 24 and 36 months (in the case with the longest follow-up), except when a complication made additional assessments advisable.

In each assessment, uncorrected visual acuity, refraction and corrected visual acuity were measured. Endothelial cell density with Topcon mirror microscope was measured after 1 week, 3, 12, 24 and 36 months; the data corresponding to this variable shown in this study are those of the last assessment of each patient. The donor disc central thickness was measured by optic coherence tomography (Visante, Carl Zeiss, Jena, Germany) 1 month after surgery. The data were included in an Excel table and subsequently processed with the SPSS statistical program (SPSS v. 17. Inc. v. 17.0. Chicago, IL, USA). The analysis included mean contrast (to determine the existence of significant differences before and after the surgical intervention) utilizing the following parametric methods: T test at 95% (α = 0.95) for independent samples (this analysis was utilized as pre-test), T test at 95% (α = 0.95) for related samples (as the variables were measured before and after the intervention) and single factor ANOVA variance analysis (α = 0.95) (to confirm or discard the results obtained in the previous test). The nonparametric tests of Wilcoxon, Friedman and Kendall (α = 0.95) were utilized to verify the homogeneity of the variables before and after the treatment.

Surgical technique

The surgical technique has been extensively described in many papers.1–5 It is necessary to operate over a button with scleral roller adapting to the artificial anterior chamber with an overall diameter of 16 mm. The cornea must have a white to white distance of at least 11 mm. The donor tissue is located over the artificial anterior chamber developed by Ziemer Ophthalmic Systems AG (Switzerland) for the Amadeus II microkeratome. No pachymetry was performed prior to the incision. In all cases a 450 μm head was utilized for obtaining
a complete anterior stroma disc providing a posterior stroma substrate of between 100 and 200 μm. After obtaining the donor disc, the button is placed over the Hessburg-Barron trephination system with the endothelium facing upwards. In this way, a disk comprising posterior stroma, Descemet's membrane (DM) and endothelium is obtained. Subsequently, the receiver corneal epithelium is marked (after applying retrobulbar anesthesia to the receiver eye and dilating with cycloplegic and phenylephrine) with the same punch utilized for trephining the donor cornea (stained with Gentian violet): this mark, with its center in the pupil, allows an adequate positioning of the donor lamella. Two paracentesis are generally performed to manipulate the donor cornea with less trauma and subsequently phacoemulsification was performed in the usual manner (when necessary), trying to penetrate through the meridian with the largest curve in order to reduce the patient astigmatism.

After introducing the IOL, the anterior chamber is pressurized with viscoelastic. If phacoemulsification is not performed, viscoelastic is utilized anyway for pressurizing the chamber. With the pupil dilated, sufficient fundus reflection is obtained to perform descemetorhexis: DM is marked and detached at 360° below the line made with the punch in the epithelium. This maneuver can be performed with custom instruments designed by multiple authors (Sinskey Katena hook [K3-5002. Katena Products, Inc., Denville, NJ, USA] oriented in the opposite direction to normal. Once the DM is detached in the periphery, its extraction can be finalized with John tweezers (AE-4962. Asico LLC, Westmont, IL, USA). Subsequently, utilizing the same instrument used for marking the DM, the posterior stroma is scraped at 360° and with a width of 1.5 mm inside the substrate left by the descemetorhexis. This maneuver exposes the posterior stroma fibers in the periphery which greatly enhances the adhesion of the donor disc in that area. Aspirating all the viscoelastic from the anterior chamber, the pupil is closed with acetylcholine and the main incision is extended to 5 mm. At this time, the donor disc is introduced in one of the several modes. In the first 6 cases we utilized the technique based on folding the lamella in the style of a Mexican taco and introducing it with tweezers. However, the technique utilized in the last 69 patients involved a sort of injector-glider designed by Maximo Busin (ref. 19098. Moria SA, Anthony, France). In this case a 2-3 mm incision must be made opposite to the main incision. Through one of the supporting paracentesis, an AC holder is introduced. After this, the donor lamella is deposited in the substrate of the glide with the endothelium facing upwards. Utilizing Busin tweezers (ref. 20004. Moria SA, Anthony, France), we pull up from one of the edges until it appears through the end of this device, which is rotated 180° and brought closer to the main incision. The same tweezers are introduced through the opposite incision and led to traverse the entire anterior chamber until its end appears through the main incision. At this point, the edge of the donor disc is caught by the tweezers and with an opposite movement the lamella is introduced in the CA. Without air assistance it unfolds due to the pressure of the AC support which is withdrawn after completing this maneuver. To obtain a definitive adhesion to the stroma, a bubble of air is injected through the opposite paracentesis and the donor lamella opens and remains adhered to the posterior stroma of the receptor. With the same instrument utilized for performing the descemetorhexis the disc can be centered in the previously marked substrate in order to pressurize the anterior chamber with air and make a stitch point in the main incision. At this time, viscoelastic is placed over the corneal epithelium and, with the aid of a thick spatula, any remaining liquid in the interface is drained (performing outward pressing movements over the corneal surface), leaving the patient in supine position for about 15 min in the surgery room stretcher. After this period, approximately 40% of the air bubble is extracted from the anterior chamber to prevent pressure surges in the immediate postop. Subsequently, the patient is transferred to a bed where he must remain motionless for at least 2–3 h to reduce the possibility of disc dislocation. The stitches were withdrawn 1 month after surgery. During the postop, prednisolone acetate and ofloxacin were utilized in the first 2 weeks and 4 h intervals, followed by 1% fluorometholone 4 times a day, diminishing the frequency of drops over a 4-month period down to once a day, maintaining the 1% fluorometholone 1 drop a day regime after the fourth month in all cases.

Results

The clinical records of the first 75 cases operated with the DSAEK technique in the La Arruzafa Ophthalmology Institute involved 67 patients (therefore, 8 were bilateral), 32 males and 35 females. All fulfilled at least 1 month of evolution: the mean ± standard deviation (range) was of 15.4 ± 10.59 (1–36) months ($M \pm SD$ [range]).

The mean age was of 66 ± 12.66 years (22–82). Four patients had failed PK (DSAEK after PK) and in 30 cases (40%), IOL implants and phacoemulsification was associated in the same operation. Eight patients were aphakic or exhibited anterior chamber lens (AC).

The most important complications during this period are summarized in Table 1. It is significant to mention that the dislocation rate was of 22.5% (17 cases); all except one were resolved with reintroduction of air in the AC. It must be taken into account that 8 patients did not have capsular support and exhibited a graft detachment rate of 50%. No dislocation occurred in prior PK cases. Five patients exhibited primary graft failure (Fig. 1). One is awaiting an additional DSAEK; another one received a PK 3 months later and the graft remains transparent with good corrected visual acuity (CVA); the remaining 3 were intervened again with DSAEK, achieving the expected visual results as in the first interventions. In 2 cases the graft failed midterm and only one case exhibited endothelial rejection (1.3%).

Five cases exhibited pupil obstruction due to air with severe hypertension. In 4 cases the obstruction was resolved by removing air in the slit lamp but, due to the said hypertension, a reactive mean midriasis persists in one case together with high IOP under treatment with carbonic anhydrase inhibitors. To date, CVA could not be recorded for this patient who before the intervention exhibited high myopia. Similarly, we have not yet been able to record the evolution of this complication, as the follow-up comprises only 1 month. While performing one of the triple procedures the posterior capsule fractured...
Table 1 – Complications in the first 75 cases intervened with automated endothelial keratoplasty with dissection of Descemet’s membrane.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of cases</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft dislocation</td>
<td>17 (22.5%)</td>
<td>50% in cases without capsular support</td>
</tr>
<tr>
<td>Primary graft failure</td>
<td>5 (6.5%)</td>
<td>2 due to surgical trauma, 2 due to inverted disc insertion, 1 due to thin lens</td>
</tr>
<tr>
<td>Reconversion to PK</td>
<td>2 (2.5%)</td>
<td></td>
</tr>
<tr>
<td>Mid-term graft failure</td>
<td>2 (2.5%)</td>
<td></td>
</tr>
<tr>
<td>Rejection</td>
<td>1 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>Pupil obstruction (due to air) with high IOP</td>
<td>5 (6.5%)</td>
<td>Non-reactive mean midriasis persists in one case</td>
</tr>
<tr>
<td>Retina detachment</td>
<td>1 (1.3%)</td>
<td>Posterior capsule rupture during surgery</td>
</tr>
<tr>
<td>Therapeutic photokeratectomy due to anterior corneal opacity</td>
<td>1 (1.3%)</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1 – (A) The primary graft failure can be observed as a striated keratoplasty with some corneal veiling which does not resolve entirely and (B) alternatively it can be seen as a severe edema both of the donor disc and in the stroma and receiving epithelium.

during the phacoemulsification, with the patient requiring anterior vitrectomy. The graft remained transparent with good CVA during 1 year but, after this period, the patient visited our practice due to loss of vision, exhibiting retina detachment with macular involvement intervened with pars plana vitrectomy and retina reattachment, achieving at this date a CVA of 0.6. In one case, a therapeutic photokeratectomy was performed 4 months after surgery in order to resolve calcium-based keratopathy, with which the patient exhibited a CVA improvement of 3 lines.

In what concerns endothelial cell loss, Fig. 2 illustrates our data. Basically, the mean cell loss was of 42.75% (Fig. 2A). In

Fig. 2 – (A) Endothelial cell loss was of 42.7% and (B) it is larger with increased surgical trauma.
addition, we recorded in the clinical records the degree of the donor endothelial trauma, i.e., null, slight, moderate or severe. Comparing the endothelial cell count in 2 groups of patients (one without traumatism or slight traumatism vs moderate or severe traumatism), obvious differences were found in the final readings (Fig. 2B). The endothelial cell loss has not been analyzed independently in the group of patients with graft dislocation.

As this is an overall analysis of a consecutive series of patients, the influence of the learning curve in the detachment rate and the possible damage of the endothelium in cases with detachment and air reintroduction have not been studied, although data on these issues are well documented in the literature. Similarly, we have not looked for differences between the Mexican taco technique and the glide introduction technique as the former has been utilized only in 6 cases.

Discussion

Corneal disc dislocation occurs due to the loss of adherence of the donor lens to the receiving stroma. The separation of the donor disc can be seen as liquid in the interface (sometimes and OCT image is necessary to adequately observe this development), or as a specific dislocation in the anterior chamber (Figs. 3 and 4). This complication is the most frequent and typical in DSAEK, with a large variation between the published series of between 0% and 82% with a mean dislocation of 14.5%. For example, the Bascom Palmer Eye Institute (Miami, FL, USA) study found 23% dislocation in a well-documented series of 118 cases while Terry reported only 1.8% dislocation in 225 eyes intervened with the triple procedure (DSAEK + phacoemulsification + IOL) and 4% in 90 patients intervened only with DSAEK. The maneuver
utilized by Terry to minimize these developments is scraping the receiver corneal stroma periphery to produce a sort of velcro effect in the adherence between the donor lens and the receiving stroma.\textsuperscript{9} Dislocation is the most frequent complication in DSAEK and it usually occurs within the first 24 h, although some late dislocation cases have been reported.\textsuperscript{9,10} Even so, we believe that it is a less dangerous development than traumatic dislocation or simply suture dehiscence in PK. Traumatism in PK suture dehiscence can be a devastating complication for eyesight whereas dislocation in DSAEK is not immediately detrimental to eyesight and does not require urgent correction to preserve the integrity of the ocular globe (although we admit that the PK dehiscence prevalence is considerably lower). Late graft dislocation in PK can occur when removing the stitches or simply when these break spontaneously or after a shock, involving frequently the loss of the eye. Even though disc dislocation in DSAEK requires additional surgical procedures (reintroduction of air in the AC or rebubbling) in order to repair this development, it does not usually involve irreversible loss of eyesight. Even so, it must be admitted that air reintroduction procedures involve potential endothelial cell loss in the immediate postop and can also increase the risk of primary graft failure.

A dislocation rate of 22.5\% can seem high considering that in some series of this rate is of 0\%,\textsuperscript{7} although the majority of papers report between 3\% and 14\%.\textsuperscript{2,3,6,12–14} However, we also found papers with dislocation rates higher than ours.\textsuperscript{15,15,16} We believe that this high variability is due to the lack of standardization of the postop management techniques as well as variable surgical experience. The presence of liquid in the interface with the edges of the graft adhered is not considered by many authors as a true graft dislocation because this complication tends to resolve spontaneously. In our 22.5\% dislocation rate, we included many of these patients because we believe that early air reintroduction enhances recovery. Eight of our patients were aphakic or exhibited anterior chamber lens. The absence of iris-lens support in these patients means that the air introduced in the AC could move to the vitreous chamber or simply be insufficient to completely pressurize the chamber and exert the necessary pressure for the donor disc to adhere to the receptor stroma, which means that in these cases lens dislocation is a frequent development. Of our 8 cases, 4 required air reintroduction to achieve correct disc adhesion, while the remaining 4 achieved primary graft adherence with the use of continuous air infusion in the AC through an AC support and from a phacoemulsifier with Venturi system. We have not analyzed differences as regards graft dislocation on the basis of the surgical trauma degree.

We had 6.5\% of primary graft failure, while in the literature the frequency of this development ranges between 0\% and 17\%.\textsuperscript{5,12,15,16} we also commented that during the learning curve this development arises more frequently because it is directly related with an aggressive surgical technique. Therefore, we consider that our primary graft failure rate falls within predictable ranges. In addition, we found 2 cases in which the graft failed in the medium-term and, if we eliminate the primary graft failure cases, we have 97.5\% of graft survival, which is also within the range of published data.\textsuperscript{1,12,17} We had only one case of endothelial rejection (1.3\%), a percentage considerably lower than the data found in the literature.\textsuperscript{6,7,18,19}

We believe that the fact of not suppressing entirely topical corticoids in these patients (as the large majority are pseudo-phakic) could influence the low frequency of this complication. In our case, the patient had interrupted the fluorometholone eyedrops regime of his own accord and visited the practice a long time later. Accordingly, even though the episode was reverted with high doses of prednisolone acetate, the endothelial loss was large (from 1945 cells per mm\(^2\) to 658), even though the graft remained transparent. The five cases of pupil obstruction were resolved after extracting air in the slit lamp although, as commented above, one patient exhibited nonreactive midriasis. Our mean cell loss was of 42.75\% (Fig. 2A), even though we did not separate the data at month 6, 12, 24 and 36 because our sample is not very large. Simply, we recorded the latest mirror microscopy measured in each case, taking into account that in some cases this was performed after 36 months and others after 1 month. If the endothelial cell loss has been studied in the group of patients with a follow-up exceeding 1 year, the sample would have been greatly reduced. Therefore, our intention was to describe this development globally, taking into account the limitations involved in not analyzing the results in different groups on the basis of follow-up time. As commented above, it seems that the endothelial loss stabilized 1 year after surgery (this is what we observed in our patients although we cannot substantiate this data) and what can be expected after 2 years is an endothelial attenuation in the range of 40\%. This number is maintained after 5 years in the longer published series (Price, Personal Communication in the World Cornea Congress held April 2010 in Boston, MA, USA) and unpublished to date. Therefore, we believe that our numbers are within what can be regarded as foreseeable for this surgery. The differences in the amount of endothelial cells according to the surgical traumatism confirms that a careful surgical technique is an important factor to avoid severe endothelial loss.\textsuperscript{13}

To conclude, we believe that, as a surgical technique, DSAEK is not free of complications although it does not seem that these could give rise to unacceptable risks in the majority of cases. There is a clear learning curve which has a bearing on the fact that at present the most frequent complication is graft dislocation, even though this development is usually resolved with re-introducing air in the anterior chamber.

Conflict of interests

None of the authors have declared any conflict of interests.

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