Original article

Comparative study of keratoconus between Anwar’s deep anterior lamellar keratoplasty versus converted penetrating keratoplasty

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ABSTRACT

Objective: To compare outcomes between penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK) in patients with keratoconus.

Design: Retrospective cohort study.

Methods: Data of 90 DALK and 49 procedures from conversion to PK, performed by a single surgeon (R.D.) from 2006 to 2011 were analyzed. Outcomes on corrected distance visual acuity (BCVA), astigmatism, time to first refraction, pachymetry, endothelial count cell, and postoperative complications were compared between these groups.

Results: The mean age of the patients who underwent DALK and PK was 28.2 and 31.7 years, respectively (P = .17). The mean follow up for DALK and for the PK group was 14.7 and 19.4 months, respectively (P = .13). There was no significant difference between PK and DALK groups in the mean postoperative for: BCVA (LogMAR) (0.17 vs. 0.17; P = .69); refractive astigmatism (−3.19 vs. −3.01 diopters; P = .65), and time for the first subjective refraction (60.5 versus 68 days; P = .50). Main postoperative complications were 8% of endothelial rejection in PK group and 10% of deep stromal vascularization in DALK group.

Conclusions: The only differences in postoperative results between groups were stromal neovascularization in DALK group and endothelial rejection in PK group. DALK should be considered as the first option when keratoplasty is indicated in keratoconus.

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Estudio comparativo en queratoplastia para queratocono entre las técnicas lamelar profunda de Anwar (big bubble) y penetrante procedente de conversión

RESUMEN

Objetivo: El propósito de este grupo de estudio fue comparar los resultados entre los procedimientos de queratoplastia lamelar profunda anterior (deep anterior lamellar keratoplasty [DALK]) y queratoplastia penetrante (penetrating keratoplasty [PK]) en pacientes con queratocono.

Diseño: Estudio de cohorte retrospectivo.

Método: Se analizaron los resultados de 90 DALK y 49 PK procedentes de reconvención en pacientes con queratocono. Todos los procedimientos fueron realizados por el mismo cirujano (R.D.) desde 2006 hasta 2011. Entre ambos grupos se comparó la agudeza visual a distancia corregida (AVCC), el astigmatismo, el tiempo de la primera refracción, la paquimetría, el recuento de células endoteliales y las complicaciones postoperatorias.

Resultados: La media de edad fue de 28,2 años para DALK y de 31,7 años para PK (p = 0,17). El seguimiento medio fue de 14,7 meses para DALK y 19,4 meses para PK (p = 0,13). No hubo diferencia significativa alguna entre los grupos de PK y DALK en la media postoperatoria de AVCC (LogMAR) (0,17 frente a 0,17; p = 0,59), astigmatismo refractivo (3,19 frente a 3,01 dioptrías; p = 0,65) ni en el tiempo de la primera refracción subjetiva (60,5 frente a 68 días; p = 0,50). Las principales complicaciones postoperatorias fueron 8% de rechazo endotelial en el grupo PK y 10% de vascularización de la interfaz en el grupo DALK.

Conclusiones: La única diferencia entre ambos grupos fue la neovascularización estromal profunda en DALK y el rechazo endotelial en PK, por lo que el procedimiento DALK debe ser considerado como primera opción en el tratamiento de pacientes con queratocono.

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Introduction

In the last decade, penetrating keratoplasty (PK) has been the surgical treatment of choice for keratocone. The drawbacks of this procedure include prolonged visual rehabilitation, high astigmatism, suture-related complications, wound dehiscence and graft rejection.1-5 On the other hand, with repeated PK procedures, graft survival rates diminished significantly at 5 and 10 years compared to baseline PK. In addition, the visual result is frequently poorer than that of the primary graft.6

Even though PK is still the most commonly applied keratoplasty procedure for treating keratocone, recent studies comparing PK with the lamellar procedure suggested that deep anterior lamellar keratoplasty (DALK) should be the first choice of treatment.7

New deep lamellar dissection techniques have been introduced in recent years.8-11 In these techniques, the stroma is withdrawn as deeply as possible, denuding Descemet’s membrane and endothelium, as in Anwar’s successful ‘big bubble’ technique.10

DALK has the advantage of preserving the receiving endothelium, thus avoiding endothelial rejection due to immune response as well as complications associated to the use of steroids for prevention and treatment.12 This technique avoids or minimizes complications related to intraocular procedures such as expulsive hemorrhage, endophthalmitis, anterior peripheral synechiae and angle closure secondary to glaucoma.9 There is increased evidence that DALK could be a safer alternative to PK even without demonstrating better visual results13,14 when executed adequately with deep dissection.15 Finally, DALK would be more useful for preserving ocular structural integrity in the presence of trauma.16,17

In addition, some authors have stated that the growing use of the lamellar technique could be beneficial in the long term, with cost savings due to the lower frequency of re-interventions and those related to the management of rejection, postoperative and intraocular complications. Said technique would be also beneficial because it increases the availability of donor corneal tissue.18,19 The main drawback of DALK is its long learning curve as it is a longer and technically more demanding procedure.1,20

As keratocone occurs in patients free of other ocular diseases and is the most common indication for DALK and PK (derived from reconvencion) in the same type of corneal condition, we believe it is the perfect situation for comparing the results of both techniques. On the other hand, considering that Reinhart et al., in their paper on DALK at the 2011 American Academy of Ophthalmology identified only 11 studies which directly compared postoperative results between DALK and PK, and indicated that all except one were level III studies and that only 7 of these included patients with keratocone but with a smaller number of cases and follow-up than the present study, the authors decided to carry out an evaluation and to report their experience with the surgical treatment for keratocone.
Patients and methods

A retrospective cohort study assessing the clinical data of 139 patients with keratocon treated with surgery between 2006 and 2011. Keratocone was diagnosed on the basis of clinical records, subjective refraction, slitlamp examination and confirmed with OPI® (Nidek®, Aichi, Japan) for assessing corneal topography. The study included patients with moderate to advanced disease, low corrected visual acuity, and intolerance or failed adaptation to contact lenses. The study excluded patients with coexisting corneal conditions or the presence of acute corneal dropsy, cataracts, retinal disorders or glaucoma.

Presurgery examination included uncorrected visual acuity (NCVA), refraction, corrected distance visual acuity (DCVA) using the Snellen table, slitlamp biomicroscopy, tonometry, ocular fundus and OPI® corneal topography to confirm keratocone grade.

The DALK group included all the successful cases of the group. The PK group included the cases that required conversion to PK.

Postoperative best corrected visual acuity was compared between both groups, together with refractive astigmatism, the time of the first subjective refraction, corneal thickness (with DGH-550 Pachette 2e pachymeter) and endothelial cell count (with Topcon SP 3000® endothelial microscope) as well as graft complications and rejections. After stabilizing suture correction either by means of extracting separate sutures or adjusting the continuous prolene 10-0 suture, the data were analyzed using the SPSS statistical application with the T for student test for group comparisons. A value of $p<0.05$ was taken as statistically significant.

Surgical technique

All the operations were performed under general anesthesia by an experienced surgeon specialized in anterior segment surgery. DALK was chosen as the first procedure in all patients, applying Anwar's 'big bubble' technique and, after assessing cone inclusion, a trephinator having a diameter between 7.25 and 8.25 mm.

PK was performed in all the eyes in which DALK could not be performed due to rupture of Descemet's membrane or because it was considered risky to place a stroma without endothelium either with micro- or macroperforations, with a lot of dissection work. Prolene 10-0 mixed sutures were used in both groups (continuous and separated). The standardized postoperative treatment in the DALK included the administration of dexamethasone and tobramycin (Tobradex®) drops during 2 or 3 months as deep corticoid penetration is not required, as well as moxifloxacin (Vigamox®) drops during one or 2 weeks, associated to a gradual regime of 1% prednisolone acetate (PredFort®) during 4–6 months in the PK group, in which deep penetration of corticoids is required for preventing endothelial rejection.

Results

Patient data

The present study included 139 eyes of 126 patients who fulfilled the inclusion criteria and comprised 49 PK procedures and 90 DALK procedures. The mean age of patients at surgery was of 28.3 years in the DALK group and of 31.7 years in the PK group ($p=0.18$). The mean follow-up time was of 36.8 months in the DALK and 48.6 months in the PK group ($p=0.13$). Graft sizes were comparable between both groups, with grafts tending to be larger in the DALK group ($p=0.06$). No differences were observed in the visual acuity recovery time, NCVA, DCVA, refractive or keratometric astigmatism between both groups. Table 1 summarizes the pre- and postoperative data of both groups.

Visual and refractive results

One year after the operation, the final DCVA (LogMAR) was of 0.15 in the DALK group and 0.17 in the PK group ($p=0.59$). NCVA and DCVA were comparable between both groups during the follow-up period. The percentage of patients with DCVA (LogMAR) of 0.3 or greater within one year was of 92% in the DALK group and

| Table 1 - summary of presurgery and post-surgery data in both groups. | Post-surgery data and results for both groups: |
| --- | --- | --- |
| # of patients (total) | 126 | |
| # of eyes per group | 90 DALK | 49 PK | T for student test | p |
| Age (years) | 28 (14 to 52) | 31.7 (14 to 83) | 0.18 |
| Graft size (mm) | 8.0 (7.50 to 8.50) | 7.75 (7.25 to 8.50) | 0.06 |
| Follow-up (months) | 36.8 | 48.6 | 0.13 |
| Time up to first refraction (days) | 60.5 | 68 | 0.97 |
| NCVA (LogMAR) | 0.59 | 0.48 | 0.21 |
| DCVA (LogMAR) | 0.15 | 0.17 | 0.59 |
| Refractive astigmatism (D) | $-3.38$ (SD 2.28) | $-3.1$ (SD 2.14) | 0.65 |
| Keratometric astigmatism (D) | $-2.94$ (SD 2.0) | $-3.28$ (SD 1.9) | 0.08 |
| Endothelial cell count (>6 months) | 1951 (SD 481) | 1470 (SD 706) | 0.01 |
| Pachymetry (um) | 545 (SD 43.35) | 547 (SD 49.8) | 0.859 |

Measured at last follow-up between 6 and 48 months.
81% in the PK group. DCVA tended to be better in the DALK group than in the PK group, as though this difference was not significant (Figs. 1 and 2).

None of the patients exhibited DCVA loss and the visual acuity improvement within one year was similar in both groups (Fig. 3).

The mean keratometric astigmatism, at least 3 months after the complete suture adjustment, was of −2.94 (−11.0 to −0.25 diopters) in the DALK group and −3.28 (−7.0 to −0.5 diopters) in the PK group. Post-surgery refractive and keratometric astigmatism assessed after one year was not significantly different between both groups (Figs. 4 and 5).

Endothelial cell count and corneal thickness

The mean endothelial cell count in the last follow-up at month 6 was a significantly higher in the DALK group (1951 cell/mm²; range: 805 a 2977) than in the PK group (1471 cell/mm²; range: 474 a 2708) (p = 0.01). The average pachymetry was very similar in both groups: 545 μ (range: 445 to 658) against 547 μ (range: 478 to 640), respectively (p = 0.859) (Table 1).

Intra- and post-surgery complications

The most frequent complication in the DALK group was conversion to PK, with a conversion rate of 37.5% (19 cases) in the first 50 cases 10% (5 cases) in the last 50 cases. Interface vascularization with penetration of vessels at a deep level, occurred in 10% of DALK group cases (Fig. 6), which were treated with the standard steroid regime. These patients did not exhibit pre or post-surgery predisposing clinical factors with the exceptions of 2 with loose sutures which were withdrawn and one patient with stroma rejection. In 2 patients, this complication was associated with lower final best corrected visual acuity due to opaque interface with lipid deposits. Temporary ocular tension occurred in 2% of DALK group cases, secondary to early postoperative injection of air in the anterior chamber to enhance graft adherence. Finally, a single case of uveitis occurred in association to stroma rejection.
Discussion

For the past 50 years, PK has been the surgical treatment of choice for patients with advanced keratocon.1,20 Recent lamellar techniques21-23 which include among others the advantages of nonpenetrating surgery24 preserve the receiving endothelium eliminating endothelial rejection caused by immune response, have strengthened the lamellar alternative for corneal conditions with healthy endothelium. Said change in grafting techniques became a new tendency to return to the techniques before PK became the surgical technique of choice on the basis of its enhanced visual results. Although PK has demonstrated to be an effective treatment for the majority of anterior segment conditions, it also involves a number of long term risks, the main being endothelial rejection and ensuing graft failure.25

In addition to exhibiting less endothelial rejection risk, said new deep lamellar techniques have less complications secondary to preventive steroid treatments such as glaucoma, cataracts, cicatization delay and infection.26 In theory, these techniques also have the advantage of virtually eliminating surgical complications from intraocular procedures such as expulsive hemorrhage, endophthalmitis, peripheral anterior synechia and secondary angle closure glaucoma.27 Finally, it has been suggested that DALK exhibits better resistance to trauma when compared to PK.16,17

DALK is the logical option for surgical treatment of keratocon and corneal stroma opacification in the presence of functional endothelium. In DALK, pathological corneal stroma is removed up to Descemet's membrane, yielding good visual results when said dissection is sufficiently deep (<100 μm), similar to the results obtained by conventional lamellar grafts.28 DALK is less invasive than PK as it keeps the ocular globe virtually closed and therefore produces less distortion of the graft bed, improved interface alignment and less postoperative astigmatism due to less sutures and adjustment thereof. These advantages became apparent in the results of the present study. Another theoretical advantage is lower risk of postoperative wound filtration and less possibility of adjustments or early suture removal, with foster visual rehabilitation. On the other hand, although this study exhibited a tendency to better DCVA in the DALK group, the results match those of other keratocone surgery studies, exhibiting none significant differences in DCVA or refractive astigmatism between both groups.24,29

Generally, the main disadvantages of DALK are its complexity, longer surgical time and slower learning curve when compared to PK.30 This match is the results of the present study, where it can be seen that the rate of macro-perforations diminished drastically from nearly 40% in the first cases to 10% in the last ones. Surgical time was also much longer at the beginning of the series, particularly when smaller bubbles formed while performing Anwar’s technique instead of a single large bubble, making it necessary to perform a careful dissection layer after layer to remove residual stroma and reach Descemet's membrane. There is no doubt that this effort was worthwhile to avoid conversion cases (which comprised the minority PK group) and thus provide a better donor-receptor optical interface in addition to eliminating the risk of endothelial immunity rejection. However, it must be noted that a bias can arise when comparing the results between the DALK and PK groups derived from a conversion, although this bias is unlikely considering that in PK the entire endothelium and Descemet's membrane are removed, just like in PK but with the only difference that it is performed in 2 phases. In any case, the longer time required for the dissection of Descemet’s membrane during the learning curve would eventually produce poorer endothelial and visual functional results than PK, which was not the case. Moreover, no evident clinical or objective differences were observed in the measurements between the first cases in which conversion was decided at an earlier phase and between the cases in which conversion was avoided due to greater experience.

The Anwar or Teichmann and Melles10,11 techniques allow Descemet membrane detachment, thus helping to avoid interface opacification and improving the possibilities of obtaining a better visual results comparable to those obtained with PK in patients without endothelial conditions.31 A further significant improvement of these techniques is the reduction of complication rates when compared to PK.32 Wound dehiscence, graft rejection, glaucoma and cataracts turned out to be more frequent in the PK group. However, attention must be paid to the increase of reported cases and longer follow-up periods after lamellar procedures as the complication rate could increase, for instance stroma rejection and interface vascularization with secondary lipidic infiltration.33

In the present study, interface vascularization occurred in 10% of cases. The histopathological study of one of these cases, prepared by Dr. Arturo Espinoza and reported by Drs. Phil Luthert and Caroline Thaung of the Moorfields Eye Hospital is of particular interest as they conclude that “the appearance, instead of being that of rejection, is more suggestive of non-specific inflammation and vascularization. This inflammation is unusual for patients with previous keratocone without the existence of pathognomonic histological rejection findings such
as clear marks of inflammatory cells along the graft-donor interface” (Fig. 6).

In this regard, it is important to point out that the authors have experienced a higher percentage of cases with interface vascularization than in other studies, some of which developed opacification secondary to lipids filtration, which could be related to stroma rejection, although clear clinical evidence or explanations were not found in all cases.

The results of the present study match those of other studies comparing DALK and PK in patients with keratoconus, without differences between groups in what concerns DCVA, refractive astigmatism or visual acuity recovery time, although with improved endothelial cell counts. The latter difference between the 2 groups of the present study can be explained by the fact that all the corneas were obtained from the eye Bank of San Diego, United States, and grafted several days after reception. Accordingly, the final endothelial reserve was diminished and unimportant. It is interesting that both groups exhibited similar post-surgery corneal thickness, which demonstrates that excellent stromal dissection and depth was achieved in the DALK group.

In conclusion, even though the optical and visual results of DALK and PK for keratocone treatment are comparable, the lower rate of graft rejection, lower use of corticoids and lower rates of associated complications, as well as a tendency toward a better DCVA, astigmatism and visual rehabilitation time, definitely make DALK the first option when keratoplasty is indicated for keratoconus. This option fully justifies the greater effort and longer learning curve involved in the procedure.

Notwithstanding all the above, additional studies including higher number of patients and longer follow-up periods would be very useful to confirm the results and long-term complications of DALK.

Conflict of interests
No conflict of interests has been declared by the authors.

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