Stromal Rejection after Deep Anterior Lamellar Keratoplasty (DALK) - A Retrospective Study

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Abstract

**Aim:** To report and analyse the incidence of stromal rejection, which is a central island of flattening of the graft associated with thinning in patients who underwent DALK for keratoconus.

**Materials & Methods:** Retrospective review of patients who underwent DALK for progressive keratoconus from 2010 to 2013 was done. Patients who completed 2 years of follow up were included. Slit lamp findings, corneal topography and central corneal thickness were analysed. 122 eyes of 71 patients were analysed. Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) were analysed in each visit

**Results:** Thirty one eyes of thirty one patients showed topographic evidence of Central Island of flattening which correlated with slit lamp finding of stromal haze of varying density. The pachymetry reading of the central cornea varied from 400 to 479µ and correlated with topographic finding of flattening. The average onset of central stromal haze was at 9 months post DALK. None of the patients had bilateral involvement. The central haze progressed over time and was associated with thinning of the cornea. The onset and progression of central flattening was associated with corresponding decrease in UCVA and BCVA. No epithelial defect was noted.

**Conclusion:** 25.4% of keratoconus patients who underwent DALK developed a central island of flattening with associated decrease in the visual acuity. The central haze, flattening and thinning may be a chronic stromal rejection or progressive thinning of cornea associated with disease process of keratoconus.

**Keywords:** Keratoconus; DALK; Stromal rejection

**Key Messages:** Stromal rejection after DALK.

**Abbrevations:** UCVA: Uncorrected Visual Acuity; BCVA: Best Corrected Visual Acuity; PK: Penetrating Keratoplasty; DALK: Deep Anterior Lamellar Keratoplasty; CCT: Corneal Pachymetry

Introduction

Keratoconus is a degenerative, non-inflammatory corneal disorder characterized by progressive stromal thinning and ectasia. 10-20% of keratoconus patients requires surgical intervention in advanced stage in the form of either Penetrating Keratoplasty (PK) or Deep Anterior Lamellar Keratoplasty [1]. Deep Anterior Lamellar Keratoplasty (DALK) is preferred over PK due to less incidence of graft failure [2]. Visual outcome of DALK surgery is comparable to PK, avoiding risk of endothelial rejection. Endothelial cell loss was low and cell count was stable after 6 months [3]. Watson et al. [4] compared DALK with PK. Best corrected visual acuity, refractive results and complication rates are similar after DALK and PK. Compared to PK, one of the major advantages of DALK is normal endothelial cell counts postoperatively. Comparatively DALK has endothelial cell loss of 1.2% at 2 years. Cell survival after DALK may be expected to be better than PK [5]. In spite of refractive stability obtained during the first years after PK for keratoconus, increasing astigmatism thereafter suggests that there is a progression of the disease in the host cornea [6]. Recurrent keratoconus following PK is rare but has been described [7-8]. N Patel has reported the first case of recurrent ectasia in a relatively new treatment option-deep lamellar keratoplasty for keratoconus [9]. We in our study have analysed post DALK patients for any such changes after two year of follow up.

**Material and Methods**

Retrospective analysis 122 eyes of 71 patients who underwent DALK for progressive keratoconus. Inclusion criteria were patients who underwent DALK for keratoconus from 2011 to 2013 and those who completed 2 years of follow-up after obtaining approval from institutional review board and ethical
had bilateral involvement. The central haze progressed over years of age, no sex association was noted. None of the patients age below 25 years with 60% cases with stromal haze below 25 post DALK (Figure 1). Haze was more common in the younger average onset of central sub epithelial haze was at 9-12 months with slit lamp finding of sub epithelial haze of varying density. The topographic evidence of Central Island of flattening. It correlated (range 15-40) years. 31 eyes of 25 patients (25% of total) showed were operated. Mean age at the time of surgery was 26.2±7.8

Statistical Analysis

Significance was assessed at 5 % level of significance. Paired t-test was used to compare pre- and postoperative astigmatism and BSCVA values and Chi-square test was used for comparison of qualitative parameters.

Results

A total of 122 eyes of 71 patients with progressive keratoconus were operated. Mean age at the time of surgery was 26.2±7.8 (range 15-40) years. 31 eyes of 25 patients (25% of total) showed topographic evidence of Central Island of flattening. It correlated with slit lamp finding of sub epithelial haze of varying density. The average onset of central sub epithelial haze was at 9-12 months post DALK (Figure 1). Haze was more common in the younger age below 25 years with 60% cases with stromal haze below 25 years of age, no sex association was noted. None of the patients had bilateral involvement. The central haze progressed over time (Figure 2a & 2b) and was associated with thinning of the cornea. These 31 eyes with stromal rejection (study group) were compared with other eyes (91 eyes) with absence of thinning or haze (control group). Mean UCVA was 0.7±0.3LogMAR in control group while in study group it was 0.88±0.15LogMAR (P<0.005). Mean BSCVA in control group was 0.19±0.18LogMAR while in study group it was 0.62±0.11LogMAR (P<0.001). The onset and progression of central flattening was associated with corresponding decrease in UCVA and BCVA. Mean keratometry in study group was K flat 40.81±1.41D and K steep 44.12±1.45 D while in control group it was K flat 45.38±2.72 D and K steep 44.12±1.45 D. Mean pachymetry reading in study group was 443.48±16.45µm while in control group it was 535±16.45µm. The pachymetry reading of the central cornea varied from 400µ to 475µm and correlated with topographic finding of thinning (Figure 3a & 3b) (Table 1). Pentacam images also showed central flattening (Figure 4a & 4b). Anterior segment OCT also showed stromal haze at periodic follow up (Figure 5a & 5b). No graft surface complications were encountered.

Discussion

Mohammad Ali Javadi et al. [11] listed the causes of decreased vision after DALK. Which includednon-endothelial graft rejection, astigmatism filamentary keratitis, vascularization. Recurrence of keratoconus in a donor cornea has already been described [12-14], and may well be manifestation of the same mechanisms that caused ectasia of the host cornea in the first place. This could be due to degradative enzymes liberated by abnormal host epithelium or infiltration of the graft by abnormal host keratocytes that produce abnormal collagen [15-16]. One speculative mechanism is failure to completely excise the cone before PKP which may lead to progression of keratoconus in the host tissue with possible involvement of the donor [17-18]. Feizi S et al. [19] reported a case of recurrence of keratoconus in corneal graft after DALK. Till now no study has shown the flattening of graft with stromal haze in late post operative period. In our study,
Figure 3: Topography showing central flattening.
Figure 4: Pentacam showing area of central flattening.
inverse keratoconus was recorded in eyes after 2 years after deep lamellar keratoplasty and this was confirmed both clinically and topographically. Stromal rejection i.e, central haze, flattening and thinning in the graft after DALK for keratoconus (Figure 4 & 5) may be chronic stromal rejection or progressive thinning of cornea associated with disease process of keratoconus or due to reduced corneal sensations. In contrast to PK, keratoconus recurred a few years after DALK. Such earlier recurrence can be attributed to several differences pertaining to the DALK surgical technique. First, retained keratocytes in the stromal bed may invade and replace donor tissue leading to recurrent keratoconus much earlier than what is expected in PK. We previously reported that even after successful big-bubble formation, some posterior stroma containing abnormal keratocytes remains in place [20]. Second, removal of DM from the donor cornea, a common practice in DALK, can theoretically weaken donor tissue. Although our comparison of graft biomechanical properties between bare-DM DALK and PK in keratoconic eyes failed to demonstrate a significant difference [21]. DM removal may actually yield donor tissue with less strength resulting in earlier manifestation of ectasia when keratoconus recurs in the DALK graft. The inflammatory pathways activated following DALK failure due to infection, in particular the metalloproteinase system (gelatinolytic activity of stromal collagenase (matrix metalloproteinase-1 (MMP-1)), may play an important part through thinning of the stromal tissue [22].

**Conclusion**

In our study the pathogenesis of corneal haze, flattening and thinning complication was unclear. Donor factors include the

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Table 1: Showing various parameters in control and study groups.

<table>
<thead>
<tr>
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<th>Control (n=91)</th>
<th>Study (n=31)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Haze</td>
<td>0.00</td>
<td>1.71+/-0.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>K flat (D)</td>
<td>45.38+/-2.72</td>
<td>40.81+/-1.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>K STEEP (D)</td>
<td>45.55+/-2.84</td>
<td>44.12+/-1.45</td>
<td>&lt;0.005</td>
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<tr>
<td>UCVA (Log MAR)</td>
<td>0.7+/-0.33</td>
<td>0.88+/-0.15</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>BCVA (Log MAR)</td>
<td>0.19+/-0.18</td>
<td>0.62+/-0.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pachymetry</td>
<td>535+/-16.45</td>
<td>443.48+/-13.58</td>
<td>&lt;0.001</td>
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Figure 5: AS-OCT showing progressive increase in the haze.
possibility of ectatic disease which may have been missed or remained subclinical throughout the donor’s life. New screening methods utilizing the Orb scan are being explored looking at the topography of donor corneas that could prevent potential problems with using ectatic corneas if routinely employed [23]. In summary, a central island of flattening after DALK with associated decrease in the visual acuity can be a chronic stromal rejection or progressive disease process of keratoconus for which we need to further investigate.

References