Therapeutic Options for Patients with Bilateral Limbal Stem Cell Deficiency

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Purpose: Live-related conjunctival-limbal allografting (Lr-CLAL), allogeneic cultivated limbal epithelial transplantation (allo-CLET), autologous cultivated oral mucosal epithelial transplantation (COMET) and Boston Type 1 Keratoprosthesis (Boston Kpro) are the four most widely performed procedures for patients with bilateral limbal stem cell deficiency (LSCD) with wet ocular surfaces. This study aimed to compare the visual outcomes of the various treatment modalities for bilateral LSCD. Methods: This was a retrospective analysis of a single surgeon’s clinical experience of treating 62 eyes of 50 patients with bilateral LSCD with wet ocular surface, over a period of ten years (2001 to 2011). The primary outcome measures were best post-operative best corrected visual acuity (BCVA) achieved and duration for which it was maintained. Results: Although mean pre-operative BCVA was comparable among the four groups (Lr-CLAL n=11, allo-CLET n=31, COMET n=13, Boston Kpro n=30) (P=0.07), post-operatively statistically significant improvement in mean BCVA was seen only after allo-CLET (0.9 logmar. P=0.0002) and Boston Kpro (1.5 logmar. P<0.0001). Mean post-op BCVA decreased after COMET, although it was not statistically significant (P=0.56). Duration for which best BCVA was maintained was similar among all groups (P=0.1). When compared head to head, proportion of patients achieving 20/200 or better vision was higher after Boston Kpro (P=0.03) as compared to allo-CLET although the duration for maintaining the same was not significantly different (0.12). Conclusions: Best post-operative BCVA attained by eyes treated for bilateral LSCD was significantly better after Boston Kpro implantation and this was maintained for as long as that following the other treatment modalities.

Damage to the corneal limbus, by injury or disease, leads to limbal stem cell deficiency. The situation becomes all the more challenging when the injury/disease is bilateral. The management of bilateral limbal stem cell deficiency (LSCD) has undergone lot of change and advancements in the last two decades. Initially, direct limbal transplantation from cadaveric or living donors was the standard of care which later evolved into cultivated allogenic transplantations so as to reduce the amount of the donor tissue required. Allogenic limbal transplantation has been used effectively over the years with success rates ranging from 50 to 100% reported by various authors. An important consideration with the same is the use of lifelong
immunosuppression with its potential side effects. To avoid the same, the autologous option in the form of cultivated oral mucosal epithelial transplantation (COMET) is also performed by few surgeons. Recently, with the introduction of Boston type 1 Keratoprosthesis (Boston Kpro) there is yet another modality for the management of bilateral LSCD that we have in our armamentarium. The practice patterns over the years have changed but to the best of our knowledge, there is no study directly comparing the outcomes of these procedures with each other. This is the first report to date comparing the outcomes of the three procedures with each other.

**MATERIALS AND METHODS**

This was a retrospective, interventional, comparative, case series of 108 procedures performed by a single surgeon at a tertiary level referral institute between 2001 and 2011 (conjunctival limbal allografting (CLAL) = 12, allogeneic cultivated limbal epithelial transplantation (Allo-CLET) = 24, COMET = 21, Boston Kpro = 51) in 90 eyes of 78 patients. All patients included in this study had clinically diagnosed bilateral LSCD (defined as 360 degrees loss of limbal palisades with either conjunctivalization or persistent epithelial defects on the corneal surface) with wet ocular surfaces (defined as a Schirmer’s 1 test score of more than 5 mm at 5 minutes). Those with severe dry eye disease or keratinization of the ocular surface; and patients with less than 6 months of post-operative follow-up were excluded from this study. Patients with lid deformities or inadequate closure, underwent corrective surgeries prior to either cell based procedures or Boston Kpro.

The primary outcome measures were compared between the four treatment groups, namely, CLAL, Allo-CLET, COMET, and Boston Kpro. The primary outcome measures were: a) Best post-operative best corrected visual acuity (BCVA); and b) duration for which the best BCVA was maintained (a loss of more than 2 lines of BCVA was considered as deterioration).

All adverse effects in both recipient and donor eyes, where appropriate, were recorded in the medical records. Failure of cell based therapy for LSCD or recurrence of LSCD was defined as re-appearance of conjunctivalization of persistent epithelial defects on the corneal surface. All suspected cases of microbial keratitis or intra-ocular infection underwent a diagnostic sampling (corneal scraping or vitreous tap/biopsy) and a complete microbiological work-up.

Patients were seen on post-operative day 1, week 1, month 1 and at two to six weekly durations thereafter depending on the clinical condition of the eye.
RESULTS

The mean age of the patients at the time of initial presentation was 33 ± 14.70 years and the male to female ratio was 31:14. Of the 90 eyes, the cause of bilateral LSCD was ocular burns in 73 eyes, multiple ocular surgeries in 8 eyes, Vernal Keratoconjunctivitis (VKC) in 6 eyes, unknown in 3 eyes. The pre-operative (baseline) LogMAR BCVA was comparable among all 4 sub-groups (CLAL=2.5±0.7, Allo-CLET=2.1±0.8, COMET=1.9±0.9, Boston Kpro=2.2±0.5, P=0.07). A significant improvement in BCVA from baseline was seen in eyes undergoing CLAL (1.3±0.8, P=0.04), Allo-CLET (1±0.9, P<0.002) and Boston Kpro (0.67±0.8, P<0.001) but not following COMET (2.3±0.6). There was no significant difference in the duration for which the best BCVA was maintained post-operatively between the four groups (CLAL= 15±0.9 months, Allo-CLET 34±13.2 months, COMET= 9±0.6 months and Boston Kpro=15±0.7 months, P=0.4).

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Pre-op BCVA</th>
<th>Post-op BCVA</th>
<th>Duration (months)</th>
<th>Significance</th>
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</thead>
<tbody>
<tr>
<td>CLAL</td>
<td>2.5±0.7</td>
<td>1.3±0.8</td>
<td>15±9</td>
<td>P=0.04</td>
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<tr>
<td>Allo-CLET</td>
<td>2.1±0.8</td>
<td>1±0.9</td>
<td>34±13.2</td>
<td>P&lt;0.002</td>
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<tr>
<td>COMET</td>
<td>1.9±0.9</td>
<td>2.3±0.6</td>
<td>9±6</td>
<td>P=0.6</td>
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<tr>
<td>Boston Kpro</td>
<td>2.2±0.5</td>
<td>0.67±0.8</td>
<td>15±7</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Significance</td>
<td>P=0.07</td>
<td>P=0.03</td>
<td>P=0.4</td>
<td>NA</td>
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DISCUSSION

In summary, the study results indicate that in terms of visual improvement and maintenance of good vision, the Boston Kpro performed slightly better than allogeneic limbal transplantation (CLAL or CLET, with or without PK) and significantly better than COMET. Although early visual rehabilitation is expected with Boston Kpro, complications like infection, glaucoma and extrusion can adversely affect the long-term visual outcomes. Our study shows that contrary to these apprehensions patients with Boston Kpros can be expected to maintain their best vision for just as long as patients undergoing allogenic limbal transplantation. These finding however need to be viewed in the context of the limitations of a retrospective study design. The results of this study can be extrapolated to patients with bilateral LSCD with wet eyes, who have undergone prior corrective lid surgery when needed. It cannot and should not be applied to patients with dry eye disease or uncorrected lid abnormalities or ocular surface exposure. This study is novel to the extent that it compares the visual outcomes of different reconstructive procedures, in patients with similar degrees of ocular surface damage, performed by a single surgeon over a decade long period. Individual results of CLAL,1-8 Allo-CLET,9-11 COMET12-19 and Boston Kpro20-26 are comparable to previously published series.
This study tried to answer the question: which therapeutic modality among allogeneic (CLAL and Allo-CLET) and autologous (COMET) cell-based approaches and Boston Kpro is better in terms of visual improvement for patients with bilateral corneal blindness due to LSCD? The findings suggest that in terms of both the best vision achieved and the duration for which it was maintained; Boston Kpro is worth consideration as a primary treatment modality for the treatment of patients with bilateral limbal stem cell deficiency with wet surfaces.

REFERENCES


