Surgical Technique

Modified Supportive Simple Limbal Epithelial Transplantation (M-SLET): A surgical technique modified for limbal stem cell deficiency

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This study aimed to develop and modify the surgical technique of simple limbal epithelial transplantation in patients with limbal stem cell deficiency to provide support to epithelial explants during the post-operative period. This is a case series of five eyes of five patients who underwent modified supportive simple limbal epithelial transplantation (M-SLET) surgery. The health and stability of the ocular surface were assessed based on clinical slit lamp examination; they were the main outcome measures. All patients had a stable ocular surface and healed epithelium during all the follow-up visits. The M-SLET technique provides additional support to limbal epithelial explants, adhering to the cornea, thus creating a stable epithelial surface. This is particularly important when there is a risk of explants being dislodged by eye rubbing.

Key words: Limbal stem cell deficiency, modified supportive simple limbal epithelial transplantation, simple limbal epithelial transplantation

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The corneal surface is covered with a layer of transparent, non-keratinized stratified squamous epithelium. These cells have a high turnover rate and are continuously replaced with limbal stem cells.[1] Corneal epithelial dysfunction is caused by limbal stem cell deficiency (LSCD) because of severe trauma or inflammation. It clinically manifests as progressive corneal vascularization, conjunctivalization, and scarring. This leads to visual impairment and blindness.

Limbal stem cell transplantation is the procedure of choice for LSCD. The healthy limbal tissue containing limbal stem cells from a normal donor eye is transplanted into the recipient eye.[1] The donor limbal tissue can be either autologous or allogenic. In conjunctival limbal autografting (CLAU), a healthy conjunctival-limbal graft is transplanted from a healthy eye to the recipient eye of the same person. Cultivated limbal epithelial transplantation (CLET)[2] is the *ex vivo* expansion of limbal stem cells, harvested from the better eye of the patient and transplanting the same on the affected eye, which minimizes the risk of iatrogenic LSCD in the donor eye. Limbal stem cells can also be harvested from the corneoscleral rims of the cadaveric donor tissue. However, cell expansion requires a clinical-grade laboratory with regulatory approval, which is extremely expensive to build and maintain.

In simple limbal epithelial transplantation (SLET),[1] a 2 mm × 2 mm tissue is harvested from the better eye, and then the explants are placed over the human amniotic membrane (HAM), which is placed over the cornea of the recipient eye. Modified supportive simple limbal epithelial transplantation (M-SLET) is a technique in which limbal epithelial explant pieces are kept under the amniotic membrane (as compared to pieces kept above the amniotic membrane in conventional SLET) and secured with fibrin glue.

Methods

Five eyes from five patients were included in the study. Four patients developed LSCD secondary to chemical injury, and one patient developed LSCD secondary to xeroderma pigmentosa. These patients underwent M-SLET for LSCD. Visual acuity was not the primary outcome measure because some patients had underlying corneal scarring. Epithelial transplant surgeries are epithelial regenerative procedures; hence, they have a limited effect on the clarity of the underlying stroma. Therefore, further surgical intervention might be required for visual rehabilitation after M-SLET surgery. All five patients were examined and assessed for health and stability of the ocular surface based on a clinical slit-lamp examination. Fluorescein staining of the surface was performed to assess epithelial integrity at 1–3 weeks. The rest of the follow-up visits were at 1–3 months, 4–6 months, 7–9 months, and 12 months and above [Please refer Table 1]. The main outcome measures were the surface and epithelial integrity.

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All the above patients underwent M-SLET surgery after complete anesthesia check-up and routine blood investigations. Three patients underwent surgery under local anesthesia, and two patients underwent surgery under general anesthesia.

In M-SLET, a 2 mm × 2 mm area on the superior limbus was marked with calliper forceps on the donor eye. A limbal-based flap of the conjunctiva was incised, and shallow dissection was performed until 1 mm into the clear cornea. The limbal tissue was excised and placed in balanced salt solution (BSS). On the recipient eye, 3–4 mm behind the limbus, a 360-degree peritomy was performed. The vascular pannus covering the cornea was dissected. The bleeding points were cauterized. The donor limbal tissue was cut into multiple small pieces using a 15 number blade or Vanna's scissors. These limbal epithelial explants were

Table 1: Procedure carried out and follow-up outcome

Patient Number and procedure	1-3 weeks Follow-up	1-3 Months Follow-up	4-6 months Follow-up	7-9 months Follow-up	>12 months follow-up
1. M-SLET	Surface stable (BCL dropout, was replaced)		DALK for visual rehabilitation.	Graft and surface stable	
2. M-SLET with DALK	Surface stable			Surface stable	Surface stable, k-pro for visual rehabilitation.
3. M-SLET	Surface stable	Surface stable		Lost to Follow-up	
4. M-SLET	Surface stable		Surface stable		Surface stable (mild superonasal pannus)
5. M-SLET		Surface stable		Lost to Follow-up	

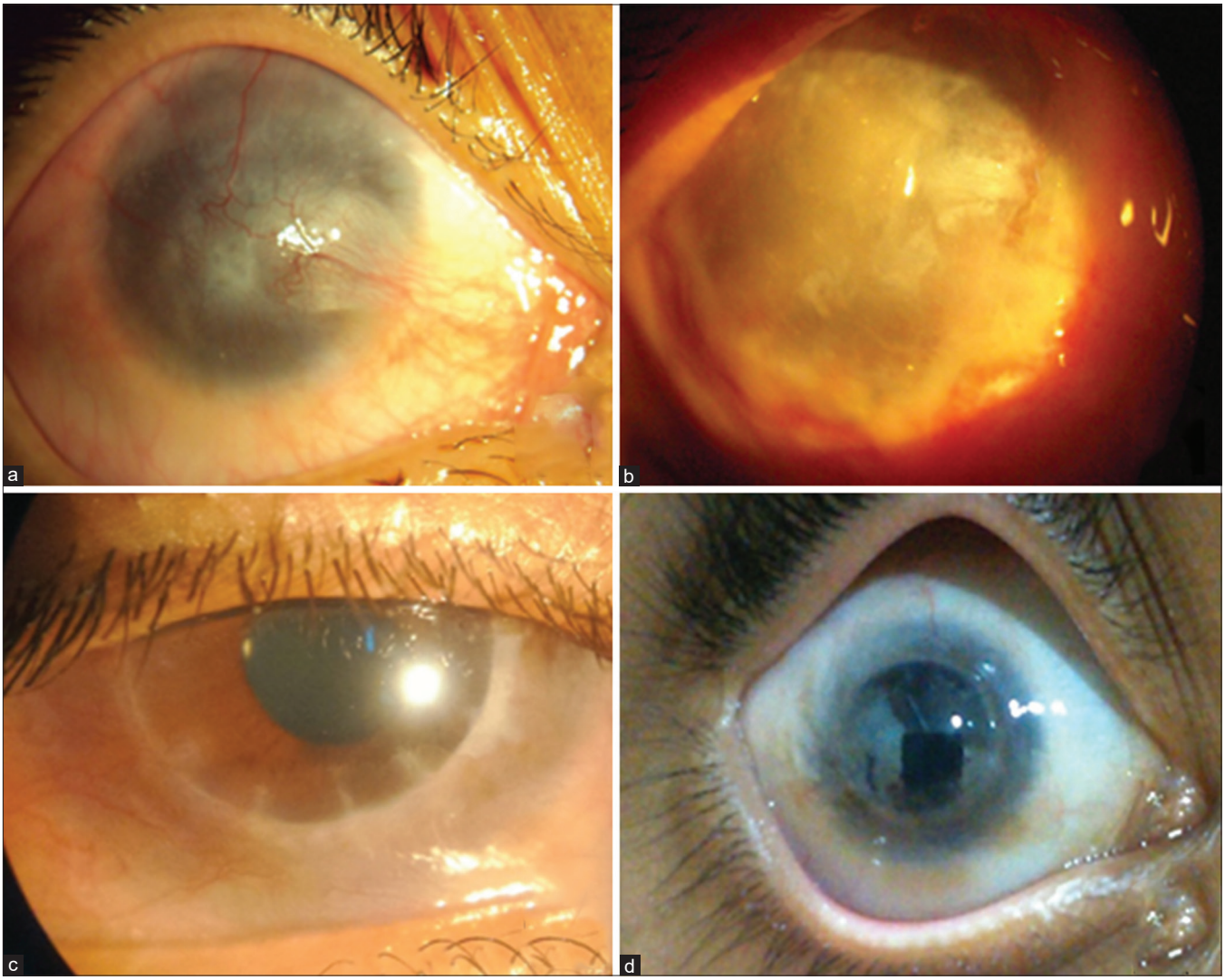

Figure 1: Patient 1: (a) Pre-operative. (b) Post-operative 2 weeks. (c)Post-operative 7 months. (d) Post-operative 10 months

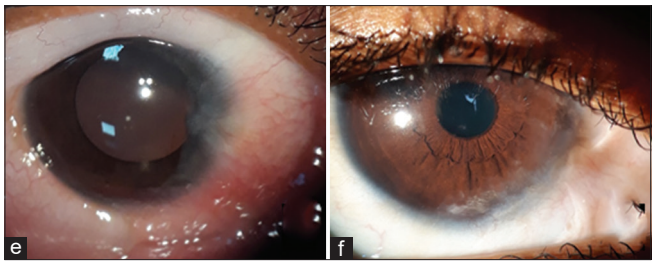

Figure 2: Patient 3: (e) Pre-operative. (f) Post-operative 6 weeks

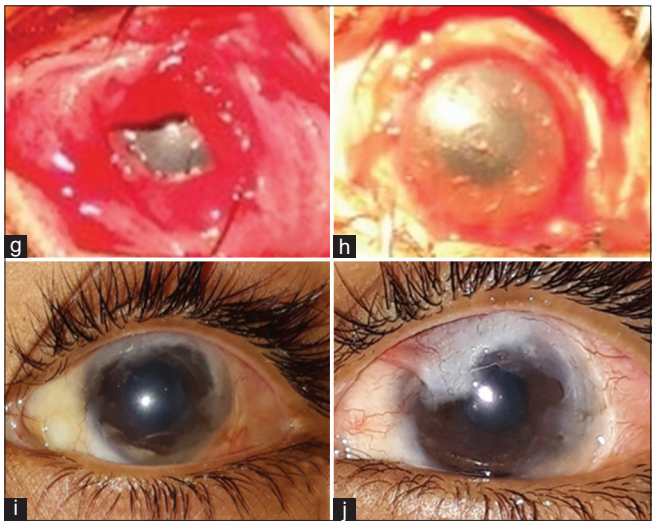

Figure 3: Patient 4: (g) Pre-operative. (h) Intra-operative. (i) post-operative 5 months. (j) post-operative 15 months

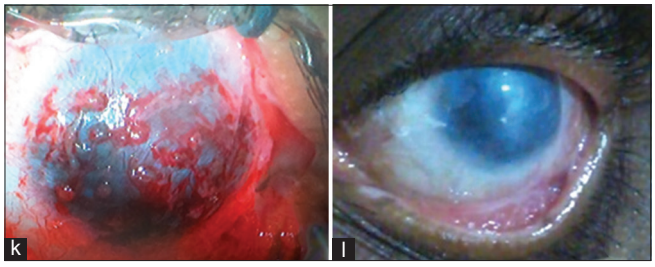

Figure 4: Patient 5: (k) Intra-operative. (l) post-operative 6 weeks

placed on the corneal surface at the mid-periphery in a circular fashion. Tissue adhesive fibrin glue was applied to the explants and the remaining bare ocular surface. HAM was placed over the explants and ocular surface. The excess membrane was trimmed, and the edges were tucked under the conjunctiva. A soft bandage contact lens was then placed over the HAM. The eye was then patched after sub-conjunctival gentamicin and dexamethasone injections. Post-operatively, the eye drops consisting of gatifloxacin (0.3% w/v) and prednisolone acetate (1% w/v) were applied 4 times a day for 1 month. Post-operative follow-up was performed on days 1 and 2. Fluorescein staining of the surface was performed to assess epithelial cell integrity at 1–3 weeks. The rest of the follow-up visits were at 1–3 months, 4–6 months, 7–9 months, and ≥12 [Table 1].

Modification

This technique was modified in comparison with conventional SLET surgery. In M-SLET, the limbal epithelial explants are kept under the HAM as compared to those kept above the HAM in conventional SLET. When limbal epithelial explants are kept under the amniotic membrane and secured with fibrin glue, it provides a good cover and support preventing the explants from getting dislodged because of accidental eye rubbing or blinking.

Results

All five patients were found to have healthy limbal anatomy and a stable ocular surface with healed epithelium at 2 weeks post-operatively, showing a healthy response to the above procedure. One patient underwent deep anterior lamellar keratoplasty (DALK) at 6 months follow-up for visual rehabilitation [Table 1, Fig. 1a-d]. The patient with xeroderma pigmentosa underwent DALK with the M-SLET procedure because of underlying corneal scarring. He also showed a stable ocular surface and good epithelial integrity until 36 months, after which he was subjected to keratoprosthesis surgery for visual rehabilitation [Table 1]. One patient with extensive LSCD because of chemical injury showed a favorable response until 15 months, after which he showed mild pannus recurrence in the superonasal quadrant [Table 1, Fig. 3i, 3j]. All patients had a healthy ocular surface and healed epithelium on subsequent follow-up visits [Table 1, Figs. 1-4].

Discussion

LSCD is the loss or deficiency of pluripotent stem cells in the limbus which are essential for the repair and renewal of the corneal epithelium. Based on the extent of involvement, it can be classified as partial or total. The SLET procedure was developed by Sangwan *et al*.[3] It does not require an extensive laboratory setup, and there is no risk of iatrogenic LSCD in the donor eye. It offers the benefits of both CLAU and CLET. A sandwich technique of SLET was described in the literature by Hernández-Bogantes *et al*.,[4] where the limbal explants were placed within the HAM fold before securing it with fibrin glue and a bandage contact lens. Amescua *et al*.[5] used a cryo-preserved amniotic membrane instead of fresh HAM for SLET. The cryo-preserved amniotic membrane was placed with the stroma side down on the ocular surface. Limbal epithelial explants are placed over it. Another cryo-preserved amniotic membrane is then placed over the limbal epithelial explants, thus sandwiching them and simulating an environment of fetal stem cells. It is described in the literature[6] that non-adherence of limbal explants on the amniotic membrane surface was one of the reasons of surgical outcome failure. In the M-SLET technique, limbal explants are more stable under the cover of the amniotic membrane and fibrin glue. There is a lower risk of losing donor limbal stem cells after BCL dropout.

The M-SLET technique provides additional support to limbal epithelial explants, helping them adhere to the cornea, thus creating a stable epithelial surface. This is particularly important when there is a risk of explants being dislodged by eye rubbing.

A limitation of this is that it was not a comparative study. The sample size was also small. As this study was conducted to establish a technique that modifies the existing surgical procedure, further studies comparing this technique with other similar surgical modalities with a large sample size need to be

conducted. This study however provides a proof of concept which could be further tested in a randomized controlled trial, comparing this technique with other similar surgical modalities with appropriate sample sizes.

Conclusion

The M-SLET technique provides additional support to limbal epithelial explants, adhering to the cornea, thus creating a stable epithelial surface. This is particularly important when there is a risk of explants being dislodged by eye rubbing.

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Conflicts of interest

There are no conflicts of interest.

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