# Allogenic Simple Limbal Epithelial Transplantation Versus Amniotic Membrane Grafting in the Early Management of Severe-Grade Ocular Chemical Injuries—A Retrospective Comparative Study

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• PURPOSE: To compare outcomes of management in the early stage of severe chemical injury (grade 4 and worse; Dua classification) with amniotic membrane grafting (AMG) alone vs allogenic simple limbal epithelial transplantation (alloSLET).

• DESIGN: Retrospective comparative interventional case series.

• METHODS: Retrospective comparative interventional series. Records of patients with severe ocular chemical injury who underwent AMG alone (between 2009 and 2013) vs alloSLET (between 2013 and 2017) were analyzed for grade of injury, time of and interventions for epithelial healing, ocular surface status post healing (grade of symblepharon, and limbal stem cell deficiency [LSCD]), and type of and need for interventions in the chronic stage.

• RESULTS: Among patients presenting in early stage of severe chemical injury, 38 eyes (median age 11 years) managed with AMG alone were compared with 39 eyes (median age 8 years) managed with alloSLET. The mean time of presentation post injury was 33.85 ± 27.5 and 40.6 ± 23.5 days in the AMG and alloSLET group, respectively. The rate of epithelial healing was faster in the alloSLET group and the difference was noted to be statistically significant (odds ratio [OR] 0.966, $P = .001$). Similarly, the lower occurrence of LSCD (OR 0.137, $P = .004$) and need for keratoplasty (OR 0.093, $P = .003$) favored alloSLET over AMG. Final best-corrected visual acuity of >20/200 was achieved in 39.4% and 53.8% in the AMG and alloSLET groups, respectively.

• CONCLUSION: AlloSLET helps in faster epithelialization of the surface, thus reducing the need for subsequent surgeries in the chronic stage and aiding faster visual rehabilitation. The outcomes of alloSLET appear superior to amniotic membrane grafting alone and should be considered in eyes with grade 4 and above (Dua classification) chemical injuries in the early stage. (Am J Ophthalmol 2020;217:297–304. © 2020 Elsevier Inc. All rights reserved.)

OCULAR CHEMICAL INJURIES ARE TRUE ophthalmic emergencies causing significant visual morbidity. Issues that need to be addressed in the acute stage include corneal/conjunctival epithelial defect, inflammation, intraocular pressure, conjunctival/limbal ischemia, and exposure, termed as the I's and E's in the management of acute chemical injury. Facilitating rapid epithelialization is of paramount significance and all the above-mentioned factors impact epithelial healing. Delay in healing of the epithelium can result in corneal melt and perforation, as well as predisposes to secondary infection. The persistence of an epithelial defect in turn further contributes to persistence of inflammation, adversely affecting residual limbal stem cells, if any, and the occurrence/degree of symblepharon.[1,2]

Joseph and associates in 2001[3] concluded that amniotic membrane grafting (AMG) did not help to restore the ocular surface or preserve the integrity of the eye in all patients with severe acute burns, when used by itself or in combination with other surgical procedures, following which Dua and associates proposed the new classification to grade chemical injuries that is being currently followed.[4] A recent randomized controlled trial in 2019 also similarly concluded that in comparison to conventional medical therapy, combined amniotic membrane transplantation and medical therapy does not accelerate corneal epithelialization or affect final visual acuity in severe (grade 4 or worse) chemical injuries, since the destruction and damage of the ocular surface is so extensive that AMG cannot overcome the extensive surface damage and inflammation, concurring with other similar trials.[5,6] The common reason for poor outcome in these studies is the delayed epithelialization and its ill effects. This clearly indicates the need for

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additional measures to promote epithelialization in severe chemical injuries.

Amniotic membrane facilitates epithelialization by acting as a basement membrane, providing epitheliotrophic and anti-inflammatory factors in eyes with adequate residual cells. In eyes with severe chemical injury with a paucity of residual cells, amniotic membrane, though it appears to be a failure, cannot provide results by itself.

The ocular surface/amniotic membrane needs to be provided with an external cell source to populate the amniotic membrane. This external source could either be autologous oral mucosal cells or allogeneic limbal stem cells. Alternate sources include autologous limbal stem cells from the opposite eye in unilateral chemical injuries or a contralateral large conjunctival autograft. Autologous limbal stem cells are not routinely indicated in the acute stage owing to the high risk of failure.[7] Cultivated oral mucosal epithelial transplantation requires advanced laboratory support and a time period of 2 weeks for the cells to be cultured, incurring further delay in the process of epithelialization.[8]

The authors have published their initial experience with allogenic simple limbal epithelial transplantation (alloSLET) in grade 4 or worse categories of the Dua classification where the mean time to epithelialization was much shorter than that reported in literature with AMG alone. In addition, a decreased incidence of symblepharon and faster visual recovery post epithelialization in the alloSLET group as compared to published reports was also noted.[5,9,10]

AlloSLET is a technique in which SLET is performed using the cadaveric limbal cells. AlloSLET is performed either for the purpose of visual rehabilitation or to hasten epithelialization of the cornea by providing an external source of corneal epithelial cells. The latter has a role to play in eyes with large areas of denuded cornea and conjunctiva following chemical injury, as described earlier. For the former, which is indicated in patients with bilateral limbal stem cell deficiency (LSCD), postprocedure systemic immunosuppression is mandatory to reduce the risk of rejection. The details of the procedure for the purpose of visual rehabilitation are outside the scope of this manuscript. With respect to the latter, the advantages of alloSLET are manifold: a larger amount of cells can be harvested from the cadaveric donor in comparison to autologous SLET (autoSLET), where the donor site is limited to 1 clock hour; limbal tissue is placed on a relatively avascular bed (midperipheral cornea), thus reducing the chances of rejection; and moreover, because the primary aim is rapid epithelialization and not long-term survival of allocells, systemic immunosuppression is not required. Over a period of time when LSCD occurs a limbal autograft can be performed 4-6 months after the primary injury in patients with unilateral chemical injuries. The primary advantage of autoSLET in unilateral injuries is the good prognosis as well as the lack of need for systemic immunosuppression, which should be availed of. In patients with bilateral chemical injury, however, systemic immunosuppression is administered following alloSLET in the acute phase in order to prolong the survival of the transplanted allocells and also to serve the purpose of visual rehabilitation.

The authors believe that with the evident benefits of alloSLET and the evident failure of AMG alone in severe grades of chemical injury, a prospective randomized controlled trial might not only be unjustifiable but also not practically feasible owing to the rarity of the condition.

The aim of this study is to highlight the benefits of alloSLET in the acute stage of severe ocular chemical injury by retrospectively comparing the outcomes of alloSLET in grade 4 or worse eyes with our own earlier experience with AMG alone for similar-grade injuries at our tertiary eye care center.

## PATIENTS AND METHODS

INSTITUTIONAL REVIEW BOARD APPROVAL WAS OBTAINED for this retrospective comparative interventional study, which adhered to the tenets of the Declaration of Helsinki. A chart review of patients in the early stage (within 1 month of onset of injury or beyond with persistent inflammation and epithelial defect) of chemical injury with grade 4 and above (Dua classification) managed with AMG alone (January 2009 to March 2013) vs alloSLET (April 2013 to December 2017) at our center was done.

Early stage was defined as presentation within 1 month of chemical injury or persistence of nonhealing epithelial defect since injury despite maximum medical or surgical intervention including amniotic membrane grafting (including beyond 1 month since the chemical injury). Hence the term "early" is used instead of acute to represent the entire spectrum of eyes that will not respond or have not responded to amniotic grafting alone.

The surgical technique of alloSLET was as described earlier by the authors and that of AMG was as described in literature. The procedure was performed preferably under general anesthesia using cadaveric limbal allograft over amniotic membrane. As fresh cadaveric tissue as possible was requested from the eye bank, preferably within 24-72 hours of harvesting. Any necrotic and nonviable tissue was excised first. Tenonplasty was performed in eyes with ischemia.[10] The amniotic membrane was draped over the entire denuded ocular surface and secured using fibrin glue and the alloSLET bits were placed only over the cornea, where they were secured with fibrin glue. Up to 4-6 clock hours of limbal tissue was harvested from the donor and cut into small pieces and placed in 2-3 concentric rows not extending up to the limbus and sparing the central cornea. A large-diameter bandage contact lens (BCL; up to 18 mm) was placed at the end of surgery. Postoperatively patients were on topical steroids (betamethasone eye drops 6 times/day), antibiotics, and lubricants,

**TABLE.** Binary Logistic Regression Between the Allogenic Simple Limbal Epithelial Transplantation and Amniotic Membrane Graft Groups

| Variables | Odds Ratio | 95% Confidence Interval | | *P* Value |
|---|---|---|---|---|
| | | Lower Limit | Upper Limit | |
| Time for epithelial healing | 0.966 | 0.947 | 0.985 | .001* |
| BCVA post epithelial healing (20/80 to 20/200) | 0.167 | 0.011 | 2.564 | .199 |
| LSCD - total | 0.137 | 0.036 | 0.526 | .004* |
| Symblepharon - grade 3 | 0.319 | 0.100 | 1.017 | .0536 |
| Symblepharon - grade 4 | 0.036 | 0.004 | 0.292 | .0018* |
| Limbal stem cell transplant | 1.063 | 0.431 | 2.618 | .895 |
| BCVA at final follow-up (20/80 to 20/200) | 0.45 | 0.094 | 2.163 | .319 |
| Leukomatous corneal opacity | 0.286 | 0.111 | 0.738 | .01* |
| Keratoplasty | 0.093 | 0.019 | 0.445 | .003* |

BCVA = best-corrected visual acuity; LSCD = limbal stem cell transplant.
Asterisks (*) indicate statistical significance.

along with systemic ascorbate 500 mg 4 times a day and systemic acetazolamide in cases with raised intraocular pressure. Systemic steroids were used in cases with severe hypotony. Systemic immunosuppression was not initiated for alloSLET eyes; however these patients were started on tacrolimus eye ointment following removal of the BCL.

• **OUTCOME MEASURES:** The primary outcome measure was the time to complete epithelialization of ocular surface from the intervention. Secondary measures included best-corrected visual acuity (BCVA), symblepharon formation, extent of LSCD, and need for keratoplasty (lamellar/penetrating) during the acute and/or rehabilitative stage of the chemical injury.

Symblepharon was graded based on classification suggested by Kheirkhah and associates.[11] LSCD was noted to be partial if there was any clock hour of intact limbus or clear corneal phenotype and total if there was 360 degrees conjunctivalization of the cornea.

• **STATISTICS:** Binary logistic regression was done for statistical analysis where the dependent variable was the treatment given (AlloSLET); 0 stands for AMG group and 1 for alloSLET. SPSS version 23 (IBM Corp, Armonk, New York, USA) was used for statistical analysis and a *P* value $< .05$ was considered statistically significant.

## RESULTS

THIRTY-EIGHT EYES OF 36 PATIENTS (M:F, 24:12) UNDERWENT AMG and 39 eyes of 37 patients (M:F, 22:15) underwent alloSLET in the acute stage of chemical injury that were categorized as grade 4 or worse based on the Dua classification. The median age was 11 years (range, 1-64 years) and 8 years (range, 2-70 years) with mean time of presentation from injury being 33.85 ± 27.5 days and 40.6 ± 23.5 days in the AMG and alloSLET groups, respectively. The cause of chemical injury was chuna/lime in 30 of 38 and 27 of 39 eyes; among the remaining, the etiologic agent was acid. Eighteen eyes (47.3%) had grade 4, 6 (15.7%) had grade 5, and 14 (36.8%) had grade 6 injury in the AMG group, with similar distribution in the alloSLET group (22 [56.4%] grade 4, 7 [17.9%] grade 5, and 10 [25.6%] grade 6 injury). Tenonplasty was performed simultaneously in 13 of 38 AMG eyes and 8 of 39 alloSLET eyes. Repeat procedure (primary) was required in 22 (52.38%) and 6 (15.38%) eyes in the AMG and alloSLET groups, respectively. It was done more than 2 times in 9 of 22 eyes with AMG but was not needed in alloSLET. Systemic steroids for hypotony were needed in 2 patients in the AMG and 1 in the alloSLET group.

Nonhealing of defect leading to stromal melt required cyanoacrylate glue application in 4 eyes, conjunctival hooding in 6 eyes, and tectonic lamellar keratoplasty in 2 eyes in the AMG group (31.57%), whereas only 3 eyes developed stromal melt requiring cyanoacrylate glue application in the alloSLET (7.6%) group. Epithelialization was achieved in all eyes, with mean time to epithelialization of 74.97 ± 38.92 days (24-164 days) in AMG group as compared to 41.2 ± 26.12 days (7-128 days) in the alloSLET group, which was noted to be statistically significant (median AMG 68, alloSLET 38).

Corneal scarring was noted in almost similar numbers of eyes, but 57.9% of eyed had a leukomatous scar in the AMG group, as compared to only 28.2% in alloSLET, which was statistically significant (*P* value .01). The majority (46.3%) had a macular scar in the alloSLET group. Similarly, the total number of eyes developing symblepharon was comparable in both the groups, but 77.7% in the alloSLET group had grade 1/2 whereas 87.5% in

AMG had grade 3/4, the difference being statistically significant (*P* value .001). Three of 38 eyes had partial LSCD while the remaining 35 (92.1%) developed a total LSCD in the AMG group. However, in the alloSLET group 3 eyes did not develop an LSCD, 12 eyes had partial LSCD, and 24 eyes (61.5%) developed total LSCD. Logistic regression for the secondary outcome measures comparing the 2 groups is mentioned in the Table.

Final BCVA of >20/200 was achieved in 15 of 38 (39.47%) AMG eyes and 21 of 39 (53.8%) alloSLET eyes, with, respectively, ≥20/60 in 6 of 15 and 12 of 21 eyes.

Of the 23 eyes with BCVA <6/60 in the AMG group, 6 were eyes of children less than 5 years of age, with 1 eye being amblyopic and the remaining 5 eyes being considered for cosmesis following multiple failed surgeries. Of the remaining 17 eyes, 4 were lost to follow-up; 2 each are awaiting stem cell transplant, lamellar keratoplasty, and fornix reconstruction; and 7 eyes were being considered for cosmesis following multiple failed interventions.

Of the 18 of 39 alloSLET eyes with BCVA <6/60, 5 eyes were of children less than 5 years of age, of which 2 eyes of 1 patient have ambulatory vision; of the remaining 3 eyes, 1 was amblyopic,1 was lost to follow-up, and 1 is being considered for cosmesis. Of the remaining 13 eyes, 3 were lost to follow-up, 4 each are awaiting limbal transplant and fornix reconstruction, 1 eye was amblyopic, and 1 had multiple failed surgical interventions.

Median follow-up was 39 and 20 months for AMG and alloSLET groups, respectively.

No eye developed a secondary infection or perforation in either group.

## DISCUSSION

THE PRIMARY GOAL OF TREATMENT IN THE ACUTE/EARLY stage of chemical injury is to facilitate rapid epithelialization, the delay of which results corneal scarring, melt, and perforation; further loss of limbal stem cells; and increased incidence of symblepharon formation.[1] Earlier studies have assessed the rate of epithelialization with the use of amniotic membrane alone and have shown it to be beneficial primarily in moderate grades of chemical injury. This concurred with our earlier experience, which pointed toward the need for providing an external source of cells in eyes with severe chemical injury.[5,10]

Corneal phenotype would be the most preferred pattern of epithelial healing, but use of limbal autograft in the acute stage is routinely not recommended. In view of the issues associated with the other sources as well as the advantage of SLET being a single-stage procedure, not requiring laboratory support, the authors have been routinely performing alloSLET for severe-grade chemical injuries since April 2013.[12]

In the present study, eyes belonging to the alloSLET group showed statistically significant faster epithelialization, the primary aim of the procedure, as compared to the AMG group. The advantages of quick epithelialization included lesser occurrence and severity of symblepharon and lesser corneal scarring.

A decreased occurrence and severity of symblepharon noted in the alloSLET group could be attributed to the faster epithelialization, which in turn assists quicker resolution of inflammation. Fifty percent of eyes had grade 4 symblepharon in the AMG group, compared to 3.7% in the alloSLET group. The need for a repeat surgery for symblepharon release was also noted to be much higher in the AMG group (37.5%) compared to alloSLET (11.11%).

The corneal scarring, which occurs because of delayed epithelial healing, was also found to be significantly less in the alloSLET group (Figure 1). Leukomatous scarring in the alloSLET group was noted only in 28.2% (11/39) (Figure 2), in contrast to 57.89% (22/38) of eyes belonging to the AMG group (Figures 3 and 4), thus reducing the need for optical keratoplasty in the chronic rehabilitative stage additionally aiding faster visual recovery. The minimal corneal haze due to the retained amniotic membrane in the alloSLET group tends to reduce.

The incidence of total LSCD was also significantly less in the alloSLET group (61.5%), in contrast with 92.1% in the AMG group. Twelve of 39 eyes in the alloSLET group had partial LSCD and 3 eyes developed no features of LSCD until the last follow-up. This could be attributed to the probable role of early resolution of inflammation because of faster epithelialization in salvaging or helping the residual host limbal stem cells to function better.

Systemic steroid was used only in patients with hypotony. This was to address the severe inflammation-related ciliary shutdown that could cause hypotony in these eyes, which could reverse with the use of systemic steroids.

Because no immunosuppression was offered, failure of the alloSLET causing LSCD was anticipated in due course. The advantage of an autoSLET not requiring immunosuppression in unilateral injuries should be availed of and retained. Hence the alloSLET in the acute stage is only a means to promote epithelialization until it eventually fails, at which time an autoSLET can be performed.

The occurrence of features suggestive off LSCD, either vascularization or conjunctivalization, partial or diffuse, encroaching toward the center of the cornea was an indication for performing autoSLET in these eyes at a minimum of 3-4 months after the acute chemical injury, following subsidence of inflammation. These ocular surface reconstructive procedures, which included symblepharon release, autoSLET, and keratoplasty (lamellar or penetrating), were in most instances performed sequentially if required. It was of interest to note that features of total LSCD occurred in fewer eyes in the alloSLET group than in the AMG group. An earlier study by the authors

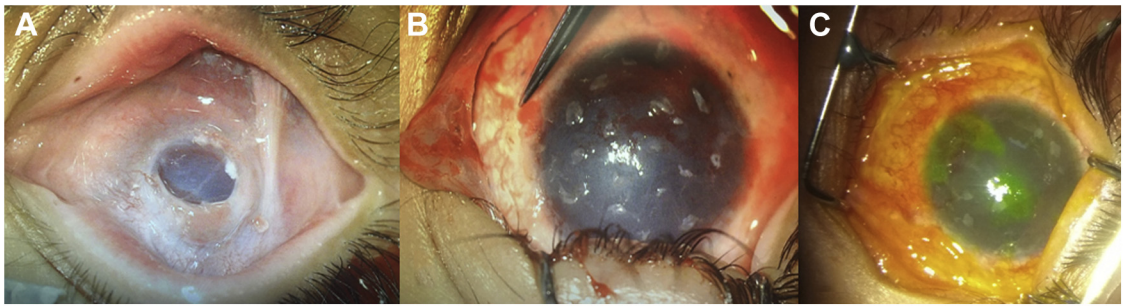


**FIGURE 1. Healing of epithelial defect with allogenic simple limbal epithelial transplantation (alloSLET). A. Central persistent epithelial defect 1 month following chemical injury after 2 amniotic membrane grafts. B. Intraoperative postsuperficial keratectomy and alloSLET. C. Three weeks later, near-total epithelialized surface.**

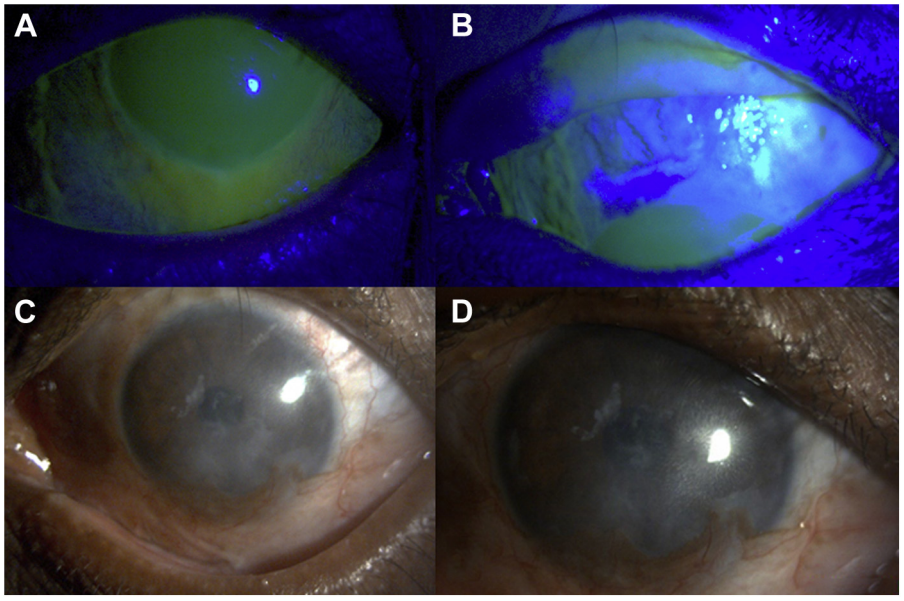


**FIGURE 2. Allogenic simple limbal epithelial transplantation (alloSLET) in acute stage: corneal phenotype with stable surface. A, B. At presentation 2 hours after chemical injury, grade 6 Dua classification. C. One month after alloSLET: epithelialized surface. D. Thirteen months after alloSLET: stable surface with corneal phenotype requiring no further intervention, maintaining best-corrected visual acuity 6/12.**

revealed chimerism in the re-epithelialized cornea following alloSLET for acute chemical injury, indicating presence and proliferation of host limbal stem cells too, in addition to the allogenic cells. Whether this reflects a protective and/or proliferative effect of the allostem cells on the host stem cells is yet to be ascertained.[9]

Following quiescence and features suggestive off alloSLET failure, SLET was performed in 16 of 38 and 17 pf 39 eyes in the AMG and alloSLET groups, respectively. Three eyes that underwent alloSLET did not develop features of LSCD (Figures 2 and 5).

Few cases (6 of 39 eyes; 15.4%) required a re-alloSLET. It is possible that the SLET bits might get dislodged in these inflamed eyes in the postoperative period and the procedure may need to be repeated more than once. A tarsorrhaphy is always placed at the end of the procedure to prevent inadvertent loss of the BCL and subsequent mechanical dislodgment of the SLET bits.

Our findings from the AMG group concur with earlier published reports. Arora and associates had reported an incidence of 60% symblepharon and 80% LSCD in 15 eyes of patients with grade 2-4 (Roper-Hall classification) when managed with AMG and medical therapy.[13] Sharma and associates have recently compared outcomes using topical umbilical cord blood, topical medications, and AMG in management of acute chemical injury with grade 3 and above of the Dua classification. Of 18 eyes managed with AMG (8 eyes, grade 3; 6 eyes, grade 4; 4 eyes, grade 5)

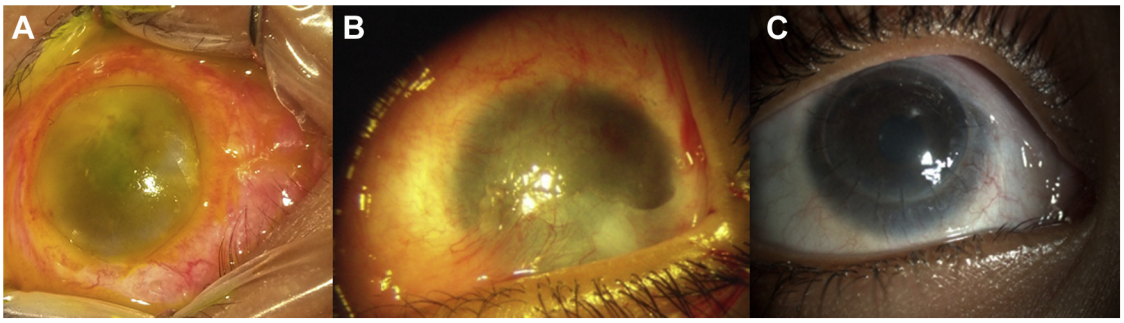


**FIGURE 3. Ex vivo limbal stem cell transplant and lamellar keratoplasty following epithelialization with amniotic membrane graft (AMG). A. At presentation 3 weeks after chemical injury: epithelial defect involving the cornea and the bulbar surface following AMG. B. Epithelialized surface with corneal scarring and symblepharon, 2 months after multiple AMG. C. Final follow-up post ex vivo limbal stem cell transplant and lamellar keratoplasty.**

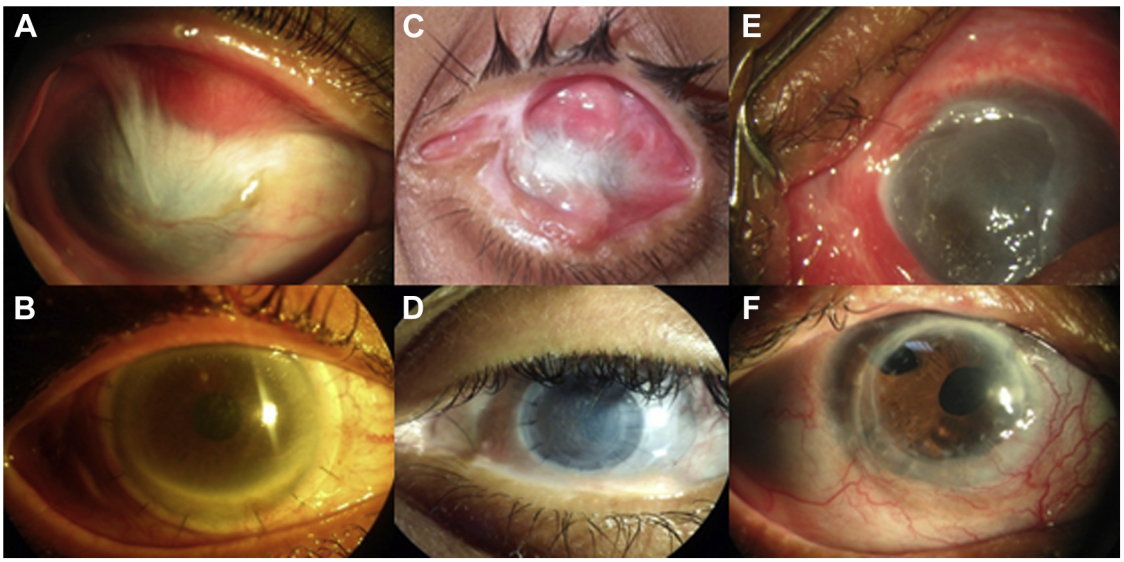


**FIGURE 4. Following epithelialization with amniotic membrane graft (AMG), multiple surgical interventions were required for visual rehabilitation. Pre (A, C, E) and final post (B, D, F) images of 3 eyes after multiple AMGs in the early stage showing symblepharon with corneal scarring (A, C) requiring lamellar (B, D) or penetrating (F) keratoplasty in the chronic stage for visual rehabilitation.**

in their study, 38% developed symblepharon and 50% LSCD despite the fact that 44.4% of their eyes had grade 3 injury.[6] Eslani and associates recently concluded that though there may be a role for AMG in moderate injuries, its role in severe cases of acute ocular chemical injury is limited.[5] It was also of interest to note that the mean and median visual acuity was 2.06 ± 0.61 and 1.79 logMAR units, respectively, when compared to our series, which was 1.12 ± 0.66 and 1 (1.51 ± 0.66; 1.8 in the AMG group), respectively, highlighting the beneficial role of alloSLET not only in faster epithelialization but also in improving visual outcomes.[5] If not the first time, the decision to perform an alloSLET as the subsequent procedure should preferably be taken if the primary amniotic membrane transplant alone fails to bring about any noticeable change in the epithelial defect in severe-grade chemical injuries.

This study, albeit retrospective with its inherent shortcomings, clearly highlights the advantages of alloSLET over AMG in the severe grades of chemical injury with very limited residual cells, conjunctival and corneal. These advantages are manifold, with not just quicker epithelialization and therefore faster subsidence of inflammation, but also lesser occurrence of symblepharon and central corneal scarring, abating the need for multiple surgeries to address these issues (including an optical lamellar or penetrating keratoplasty for visual rehabilitation). This procedure also aids in quicker visual recovery, especially in children prone to development of amblyopia. Immunosuppression does not form part of the management

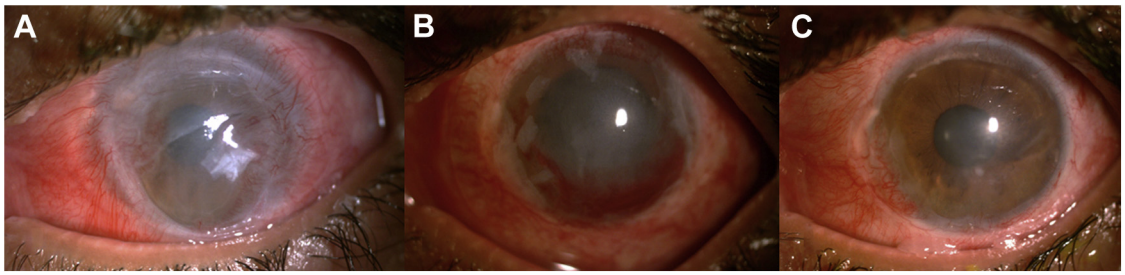


**FIGURE 5. Clear epithelialized cornea post allogenic simple limbal epithelial transplantation (alloSLET) for persistent epithelial defect (PED). A. PED 1 month after chemical injury. B. One week after alloSLET. C. One month later: epithelialized surface with clear cornea.**

protocol. The major advantage of autoSLET in unilateral chemical injuries is avoidance of immunosuppression. Long-term immunosuppression for alloSLET survival would therefore defeat this advantage. AlloSLET in this circumstance functions as a stop-gap measure until an autoSLET is performed, if required. Cadaveric limbal tissue provides cells that are of corneal phenotype, and adequate amount of cells can be harvested from the cadaveric donor. It is of utmost importance to choose fresh cadaveric tissue to ensure viability of stem cells. However in bilateral cases, autoSLET is not an option in the future; therefore, immunosuppression should be initiated to increase the survival of the transplanted allogenic cells. The immunosuppressive regimen that we have been following for such cases is systemic mycophenolate mofetil 1-1.5 grams per day, topical tacrolimus eye ointment twice a day, and tapering dose of topical steroids continued once a day, along with tapering dose of systemic steroids.

To summarize, alloSLET thus definitely appears to have a role in and should be added to the armamentarium of modalities in the management of acute severe-grade chemical injuries.

## CRediT AUTHORSHIP CONTRIBUTION STATEMENT

**SHWETA AGARWAL:** METHODOLOGY, RESOURCES, FORMAL analysis, Data curation, Writing - original draft, Writing - review & editing. **Bhaskar Srinivasan:** Methodology, Resources, Formal analysis, Data curation, Writing - original draft, Writing - review & editing. **Rishi Gupta:** Resources, Formal analysis, Data curation, Writing - review & editing. **Geetha Iyer:** Methodology, Resources, Formal analysis, Data curation, Writing - original draft, Writing - review & editing.

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Statistical analysis was done by Mr Vishwanathan Natarajan, MSc Statistics, Sankara Nethralaya, Chennai, India.

## REFERENCES

1. Wagoner MD. Chemical injuries of the eye: current concepts in pathophysiology and therapy. *Surv Ophthalmol* 1997;41(4):275–313.
2. Iyer G, Srinivasan B, Agarwal S. Algorithmic approach to management of acute ocular chemical injuries-I's and E's of management. *Ocul Surf* 2019;17(2):179–185.
3. Joseph A, Dua HS, King AJ. Failure of amniotic membrane transplantation in the treatment of acute ocular burns. *Br J Ophthalmol* 2001;85(9):1065–1069.
4. Dua HS, King AJ, Joseph A. A new classification of ocular surface burns. *Br J Ophthalmol* 2001;85(11):1379–1383.
5. Eslani M, Baradaren-Rafi A, Cheung AY, et al. Amniotic membrane transplantation in acute severe ocular chemical injury: a randomised clinical trial. *Am J Ophthalmol* 2019;199:209–215.
6. Sharma N, Lathi SS, Sehra SV, et al. Comparison of umbilical cord serum and amniotic membrane transplantation in acute ocular chemical burns. *Br J Ophthalmol* 2015;99:669–673.
7. Rao SK, Rajagopal R, Sitalakshmi G, et al. Limbal autografting: comparison of results in the acute and chronic phases of ocular surface burns. *Cornea* 1999;18(2):164–171.
8. Sotozono C, Inatomi T, Nakamura T, et al. Cultivated oral mucosal epithelial transplantation for persistent epithelial defect in severe ocular surface diseases with acute inflammatory activity. *Acta Ophthalmol* 2014;92(6):e447–e453.
9. Iyer G, Srinivasan B, Agarwal S, et al. Outcome of allo simple limbal epithelial transplantation (alloSLET) in the early stage of ocular chemical injury. *Br J Ophthalmol* 2017;101(6):828–833.
10. Iyer G, Srinivasan B, Agarwal S, et al. Visual rehabilitation with keratoprosthesis after tenonplasty as the primary

globe-saving procedure for severe ocular chemical injuries. *Graefes Arch Clin Exp Ophthalmol* 2012;250(12):1787–1793.
11. Kheirkhah K, Blanco G, Casas V, et al. Surgical strategies for fornix reconstruction based on symblepharon severity. *Am J Ophthalmol* 2008;146(2):266–275.
12. Sangwan VS, Basu S, MacNeil S, et al. Simple limbal epithelial transplantation (SLET): a novel surgical technique for the treatment of unilateral limbal stem cell deficiency. *Br J Ophthalmol* 2012;96(7):931–934.
13. Arora R, Mehta D, Jain V. Amniotic membrane transplant in acute burns. *Eye* 2005;19(3):273–278.