

Limbal stem cell transplantation in patients with chemical burns to the ocular surface

Transplante de células-tronco do limbo em pacientes vítimas de queimadura química da superfície ocular

Sacha Fernandes Pereira¹ , Manoela Alves dos Santos¹ , Davi Montenegro Leal Fernandes¹ ,
Vinícius Gomes Alves de Oliveira² , Denisse Josefina Mora-Paez³ , Dillan Cunha Amaral² , Luiza Toscano de Almeida¹ ,
Ricardo Nogueira Louzada² , Milton Ruiz Alves⁴ 

¹ Afya, Ciências Médicas da Paraíba, João Pessoa, PB, Brazil.

² Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

³ Glaucoma Research Center, Wills Eye Hospital, Philadelphia, PA, USA.

⁴ Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil.

How to cite:

Pereira SF, Santos MA, Fernandes DM, Oliveira VG, Mora-Paez DJ, Amaral DC, et al. Limbal stem cell transplantation in patients with chemical burns to the ocular surface. *Rev Bras Oftalmol.* 2026;85:e0005.

doi:

<https://doi.org/10.37039/1982.8551.20260005>

Keywords:

Chemical burns; Limbal stem cell; Cornea

Descritores:

Queimaduras químicas; Células-tronco do limbo; Córnea

Received on:

February 11, 2025

Accepted on:

October 10, 2025

Corresponding author:

Ricardo Nogueira Louzada
Instituto de Olhos São Sebastião
Largo do Machado, 54 room 1208
Zip Code: 22221-020 – Rio de Janeiro,
RJ, Brazil
E-mail: louzada@hucff.ufrj.br

Institution:

Faculdade de Medicina, Universidade
Federal do Rio de Janeiro, Rio de Janeiro,
RJ, Brazil.

Conflict of interest:

no conflict of interest.

Financial support:

no financial support for this work.

Data Availability Statement:

The datasets generated and/or analyzed during the current study are included in the manuscript.

Associate editor:

Bruno Machado Fontes
Centro de Microcirurgia e Diagnóstico. Rio
de Janeiro, RJ, Brazil
<https://orcid.org/0000-0001-5725-1458>



Copyright ©2026

ABSTRACT

Our objective was to evaluate and describe the techniques and outcomes of limbal stem cell transplantation in patients with limbal stem cell deficiency after chemical burn of the ocular surface. We performed this literature review using the PubMed® (MEDLINE), Cochrane and Embase (Elsevier) databases. Of the 313 studies found, 276 were removed as duplicates and ineligible based on the inclusion and exclusion criteria; 17 articles remained after full reading, classified according to the criteria of interest, and 1 article was included manually as it was essential for this study. After careful analysis of the literature, we identified that conjunctival limbal autograft has a higher success rate and fewer complications than conjunctival limbal allograft. Allogeneic grafts require immunosuppressive therapy; and autologous cultivated limbal epithelial transplantation, although being considered the standard of care for unilateral limbal stem cell deficiency, has the disadvantage of high financial cost. Chemical injuries were once considered an irreversible cause of blindness. There is no single treatment for all possible burns, but with all the evolution, there are several possible reversal techniques. Each case must be evaluated according to the causal factors and degree of involvement of the ocular surface.

RESUMO

Nosso objetivo foi avaliar e descrever as técnicas e resultados do transplante de células-tronco do limbo em pacientes com deficiência de células-tronco límbicas após queimadura química da superfície ocular. Realizamos esta revisão de literatura usando os bancos de dados PubMed® (MEDLINE), Cochrane e Embase (Elsevier). Dos 313 estudos encontrados, 276 foram removidos como duplicados e ineligíveis com base nos critérios de inclusão e exclusão; 17 artigos permaneceram após a leitura completa, classificados de acordo com os critérios de interesse, e 1 artigo foi incluído manualmente pois era essencial para este estudo. Após análise cuidadosa da literatura, identificamos que o autoenxerto límbico conjuntival tem uma maior taxa de sucesso e menos complicações do que o aloenxerto límbico conjuntival. Enxertos alôgenos requerem terapia imunossupressora; e o transplante epitelial límbico cultivado autólogo, embora seja considerado padrão ouro para a deficiência unilateral de células-tronco límbicas, tem a desvantagem de alto custo financeiro. Lesões químicas já foram consideradas uma causa irreversível de cegueira. Não há um único tratamento para todas as queimaduras possíveis, mas com toda a evolução, existem várias técnicas possíveis de reversão. Cada caso deve ser avaliado de acordo com os fatores causais e o grau de envolvimento da superfície ocular.

INTRODUCTION

Acute ocular burns are ophthalmic emergencies requiring immediate intensive intervention. The incidence in developing countries is reported as 1.25 to 4.4%. Visual recovery and ocular surface healing depend on the extent of the initial damage and the physical properties of the causative agent. If not adequately treated in the acute bilateral phase, chronic sequelae such as limbal stem cell deficiency (LSCD), corneal scarring, and glaucoma may develop.⁽¹⁾

The classification of chemical ocular burns is based on the extent of limbus, conjunctiva, and cornea involvement. Ocular burns generally occur at home or in the workplace, with the former being mostly mild and the latter often more severe. Preventing further damage through copious and prolonged eye irrigation, after verifying the pH of both eyes, along with exploration and removal of all particles, is essential. Intraocular pressure is often overlooked and should be assessed and controlled. Management typically requires a multidisciplinary approach.⁽²⁾

The corneal limbus contains a population of stem cells that is essential for maintaining and regenerating the corneal epithelium. Limbal stem cell deficiency, caused by either hereditary or acquired disruption of this stem cell niche, results in poor corneal epithelialization, epithelial defects, secondary corneal vascularization, stromal scarring, and/or conjunctivalization of the cornea.⁽³⁾

With more severe injuries, complete loss of the corneal and limbal epithelium occurs. This is associated with partial or “total” loss of the conjunctival epithelium. In cases with complete loss of the corneal and limbal epithelium but with some surviving conjunctival epithelium, the conjunctival epithelium migrates to cover the limbus and cornea. The conjunctival epithelium that grows over the cornea, whether with sectoral or total limbus involvement, brings blood vessels, lymphatics, and fibrous tissue, covering the cornea with a fibrovascular pannus of varying thickness. Involvement of the limbal stroma, in the form of damage, loss of epithelial stem cells, and limbal ischemia, is a crucial factor in assessing and predicting corneal epithelial regeneration. Limbal ischemia presents as whitish or pale limbus areas, limbal edema, necrotic tissue, hemorrhage, and blood columns. These changes may obscure pallor and cause underestimation of ischemia.⁽²⁾

Two prognostic classifications assess chemical ocular injury: the Roper-Hall (modified Ballen's) and the Dua classification.⁽²⁾ The Roper-Hall classification was

introduced in 1965 to facilitate COI grading and prognosis based on the extent of limbal ischemia and corneal opacity. In the Dua classification,⁽²⁾ the extent of limbal involvement is determined using fluorescein staining and/or limbal ischemia and is recorded in terms of the number of “clock hours” of affected limbus, which serves as a more objective measure. The surviving conjunctival epithelium provides vital coverage for the cornea, based on the principle that any coverage is better than none. Therefore, recording the extent of conjunctival involvement is essential in any grading system. Regarding the ocular surface, there are five main sequelae: dry eye, conjunctival adhesions/syblepharon, non-healing epithelial defects and/or neurotrophic keratopathy, LSCD, and corneal scarring, decompensation, thinning, melting, and perforation. Rapid visual recovery occurs when the corneal epithelium derived from surviving limbal cells covers the visual axis.⁽²⁾

Treatment depends on injury extent and central corneal involvement. Many patients with partial LSCD with central corneal preservation can be treated conservatively, using lubrication and autologous serum eye drops, while partial surgical management may be considered in cases with central corneal involvement. Limbal stem cell transplantation (LSCT) may be considered for patients with more extensive corneal conjunctivalization. It is not recommended during active inflammation and should be postponed until ocular surface inflammation has subsided or is well controlled with medication. Additionally, all eyelid abnormalities should be addressed before considering LSCT.⁽⁴⁾

The treatment of LSCD has evolved significantly through innovative pharmacological strategies, surgical techniques, bioengineering, and cellular therapy. This work will address some techniques for LSCT in patients with LSCD due to chemical ocular burns from the following sources: allogeneic, autologous, and ex vivo cultured.

METHODS

A literature review was conducted on LSCT in patients with ocular burns using the PubMed® (MedLine), Cochrane, and Embase (Elsevier) databases. This study was guided by the question “What are the main techniques of LSCT used in patients with chemical burns to the ocular surface?” Based on this, we defined Boolean descriptors and a search strategy with the following terms: (Transplant AND “Limbal Stem Cell”) OR “limbal stem cell transplant” AND trauma AND (“chemical” OR “chemical Injury”).

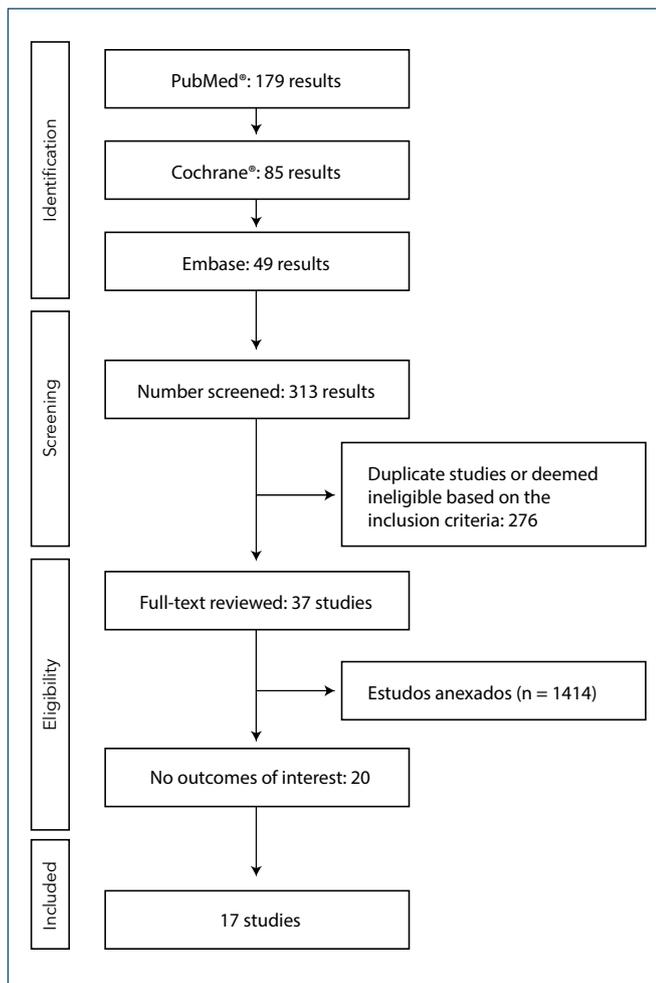


Figure 1. PRISMA 2020 flow diagram of studies included by database (2024).

For this study, we included randomized and observational studies, without restrictions on time or language. Inclusion criteria were population: patients with chemical burns; intervention: patients undergoing LSCT;

outcomes as fully epithelialized and avascular corneal surface, improvement in corneal transparency, improvement in visual acuity, and stability of the corneal surface. Exclusion criteria were studies that did not meet the inclusion criteria, studies without relevant outcomes, case reports, animal studies, paid studies, and editorials, letters, and conference proceedings without sufficient data.

RESULTS

We identified 313 studies across the databases, with 179 from PubMed®, 85 from Cochrane, and 49 from Embase. Of these, 276 were removed as duplicates or deemed ineligible based on the inclusion and exclusion criteria, leaving 37 articles for full-text review, of which 20 were excluded according to relevance criteria. Consequently, 17 studies were included in this review⁽¹⁻¹⁷⁾, as detailed in figure 1. Finally, 1 article was manually included due to their critical importance to the study results. The characteristics of each selected study are described in table 1.

General approach – limbal stem cell transplantation

Corneal blindness following ocular burns was once considered incurable, as it had a very poor prognosis for corneal transplantation. The subsequent discovery of epithelial stem cells in the limbal region of the eye demonstrated that ocular blindness was a manifestation of limbal dysfunction and could potentially be reversed by LSCT.⁽¹⁴⁾

In cases of LSCD, optimizing the ocular surface by addressing all associated comorbidities is essential prior to surgical interventions, regardless of the specific surgical strategy considered. The main objectives are to provide

Table 1. Baseline characteristics of included studies

Study	Study type	Study Characteristics
Kate et al. ⁽¹⁾	Observational study	To compare the demographic and clinical profile of acute ocular burns in children and adults
Dua et al. ⁽²⁾	Literature review	To explain the pathophysiology, assessment, and management of ocular chemical injuries
Ballios et al. ⁽³⁾	Systematic review	To evaluate the benefits and adverse effects of systemic immunosuppression used in TCTL
Baradaran Rafii et al. ⁽⁴⁾	Systematic review	To classify current and future therapies for ocular chemical injuries
Basu et al. ⁽⁵⁾	Observational study	To report the clinical outcomes of SLET in recurrent unilateral DCTL eyes due to CLET failure
Basu et al. ⁽⁶⁾	Case series	To describe the long-term clinical outcomes of SLET
Borroni et al. ⁽⁷⁾	Literature review	To review on the current approach and future directions of SLET
Campbell et al. ⁽⁸⁾	RCT	To demonstrate the feasibility and safety of bilateral CLET-al
Deng et al. ⁽⁹⁾	Literature review	Global consensus on the treatment of DCTL for autologous and allogeneic transplants
Korkmaz et al. ⁽¹⁰⁾	Observational study	To evaluate the success of TCTL in DCTL caused by chemical injury
Le et al. ⁽¹¹⁾	Meta-analysis	To evaluate the outcomes of CLAU, CLAL, CLET-AU, and CLET-AL techniques
Ramírez et al. ⁽¹²⁾	Case series	To evaluate the outcomes of CLET in treating ocular surface failure due to LSCD
Sangwan et al. ⁽¹³⁾	Case series	To describe the SLET technique
Sangwan et al. ⁽¹⁴⁾	Observational study	To evaluate the efficacy of xeno-free autologous cell-based treatment for LSCD deficiency
Shanbhag et al. ⁽¹⁵⁾	Systematic review	To evaluate the outcomes of different autologous TCTL techniques
Shanbhag et al. ⁽¹⁶⁾	Systematic review	To evaluate the keratolimbal allograft technique for DCTL following severe corneal chemical injury
Vazirani et al. ⁽¹⁷⁾	Case series	To report the outcomes of CLET-au using the affected part of the healthy eye or the contralateral eye in patients with unilateral partial LSCD
Soma et al. ⁽¹⁸⁾	Observational study	To describe a new human iPSC-based transplant surgery to reconstruct the eyes of patients with vision loss owing to an LSCD

LSCT: ex vivo cultivated autologous limbal transplantation; SLET: simple limbal epithelial transplantation; CLET: cultivated limbal epithelial transplantation; CLAU: conjunctival limbal autograft; CLAL: conjunctival limbal allograft; CLET-au: autologous cultivated limbal epithelial transplantation; CLET-al: allogeneic cultivated limbal epithelial transplantation; iPSC: induced pluripotent stem cells; LSCD: limbal stem-cell deficiency; RCT: Randomized clinical trial

the best possible ocular surface environment for the graft and long-term survival of the transplanted stem cells, enhance the survival of any remaining stem cells in cases of partial LSCD, and simultaneously improve health and symptoms. Additionally, the goal is to improve the phenotype and integrity of the damaged or diseased corneal epithelium and, subsequently, to enhance the corneal barrier function.⁽¹²⁾

The choice of surgical treatment and therapy depends on the stage of LSCD and its laterality. For eyes with significantly compromised vision and severe LSCD, surgical treatment is often necessary to stabilize the ocular surface and improve visual function. The surgical technique employed will depend on the patient's injury and may involve using healthy limbal stem cells from the unaffected eye (autologous transplantation) or donor stem cells (allogeneic transplantation), depending on whether the injury is unilateral or bilateral. Over recent decades, surgical techniques have evolved from direct limbal transplantation to ex vivo cultured limbal epithelial cell transplantation, which is safer for the donor eye, as it requires less tissue.⁽¹³⁾

Cultivated limbal epithelial transplantation

Cultivated limbal epithelial transplantation (CLET) reconstructs the corneal epithelium by culturing donor limbal tissue in vitro to allow stem cell proliferation. These cells can be sourced either autologously (CLET-au) or allogeneically (CLET-al).⁽¹²⁾ Cultivated limbal epithelial transplantation is a suitable alternative in cases of total unilateral LSCD or in cases of bilateral involvement where one eye is more severely affected. The surgical success rate of CLET may be associated with a longer interval between the chemical injury and surgery, as inflammation tends to regress over time, thereby promoting graft survival.⁽⁴⁾

Currently, CLET is accepted as the standard treatment for LSCD and is routinely practiced. Repeatability is a major advantage of CLET, as well as the small amount of tissue required, which reduces the risk of LSCD in the donor eye in unilateral cases, whether autologous or allogeneic.⁽¹²⁾ However, the primary disadvantage is the high financial cost, which limits its accessibility in developing countries, and the risk of rejection despite systemic immunosuppression.^(7,10) Treatment must be individualized for each patient, considering the etiology and severity of the disease at presentation.⁽⁹⁾

Most recently, scientific literature presented a new study that describes a new human iPSC-based transplant surgery to reconstruct the eyes of patients with vision loss owing to an LSCD. Induced pluripotent stem cells (iPSCs)

were studied in four patients with LSCD, despite the limitations, such as the low number of participants, the procedure was successful and well-tolerated two years post-operatively.⁽¹⁸⁾ The procedure grafting iPSC-derived corneal epithelial cell sheets (iCEPs) onto the ocular surface after the removal of fibrotic tissue that envelops the ocular surface, found no safety issues (clinical immunological rejection or tumor formation) throughout the whole follow-up observational period in any of the patients. At the end of the follow-up period, all four eyes also showed positive results clinically, with an improvement in the clinical stage of the disease, better visual acuity, and diminished corneal opacification. The results were achieved without the use of human leukocyte antigen (HLA) matching or immunosuppressive agents, except for corticosteroids. This could be explained by a relatively low expression of HLA class I and II, and an absence of immunocompetent cells, such as Langerhans cell, from iCEPs.⁽¹⁸⁾

Autologous limbal stem cell transplants

Conjunctival limbal autograft

From 1989 to 2006, conjunctival limbal autograft (CLAU) was the most performed procedure for severe unilateral LSCD. Studies indicate that 35% to 88% of eyes undergoing CLAU showed improvement in the ocular surface and visual acuity.⁽⁹⁾ The long-term success of autologous transplantation is attributed to the absence of immunological rejection. However, the limitation of this approach is that it requires the removal of 40% to 50% of the donor limbus, posing a small risk of iatrogenic damage to the healthy eye.^(9,17)

The CLAU procedure uses healthy eye tissue and is highly effective for unilateral LSCD, achieving regression of the corneal neovascularization and restoring vision 80% to 90% of cases.⁽⁴⁾

To reduce the potential risk of iatrogenic LSCD and trauma to the healthy donor eye, autologous ex vivo-cultivated LSCT has been employed. The main advantages of ex vivo-cultivated autologous stem cells are the minimal donor tissue required. However, the downside is that it necessitates a qualified laboratory to culture them, thus raising the costs.⁽⁹⁾

For severe unilateral LSCD, autologous transplantation should be considered the first-line surgical option, as it^(2,3,5,9,14-17) offers better long-term graft survival and avoids risks associated with systemic immunosuppression required in allogeneic transplants and the vision-threatening complications. In cases where ocular surface stem cell

transplantation fails, the cornea may become conjunctivalized and scarred, and failure of a keratoprosthesis due to complications such as endophthalmitis may result in loss of the eye. Consequently, if the unaffected contralateral eye has good visual acuity, allogeneic transplantation and keratoprosthesis use can be avoided.⁽⁹⁾

Simple limbal epithelial transplantation

Simple limbal epithelial transplantation (SLET) was first described in 2012 by Sangwan et al.⁽¹⁴⁾ when treating total unilateral LSCD, particularly when induced by chemical burns.⁽⁶⁾ In this approach, a small biopsy (equivalent to 1 clock hour) of limbal tissue is excised from the healthy contralateral donor eye and dissected into multiple pieces. An amniotic membrane (AM) is secured with fibrin glue onto the diseased eye after pannus removal and conjunctivalization of the corneal surface. The limbal biopsy fragments are placed on the AM and secured with fibrin glue, followed by a contact lens to dress the ocular surface.^(7,14)

The AM is crucial for successful SLET, providing necessary growth factors and being safe and effective in restoring partial LSCD, playing a critical role in preserving limbal epithelial stem cells. Early intervention with AM can prevent partial or total LSCD, whether using autologous or allogeneic techniques.⁽⁷⁾

The SLET technique requires minimal donor tissue, avoids lab support, and reduces iatrogenic LSCD risk, making it a simpler alternative to CLET.^(6,14) Furthermore, since it is performed in a single stage, *ex vivo* expansion of stem cells is not required, making it a more cost-effective and accessible method, providing economic advantages over other techniques.⁽¹⁴⁾

Allogeneic limbal stem cell transplantation

If the contralateral eye is not a suitable donor or if the patient prefers to avoid surgery on the healthy eye, allogeneic LSCT may be considered. Allogeneic LSCT is performed in patients with severe bilateral LSCD, where sufficient functional cells need to be restored. Allogeneic LSCT sources for patients with LSCD require tissue from a donor who may be compatible, partially compatible from living relatives, or unrelated cadaveric donors.

Compatibility may be based on blood type and/or human leukocyte antigen (HLA). However, this hypothesis remains unproven, but it is based on findings that HLA and blood-type matching in other solid organ transplants improve graft survival. It is hypothesized that blood type and HLA-compatible LSCT grafts might also yield better

long-term outcomes and lower the risk of ocular complications than incompatible LSCT grafts.⁽⁹⁾

Allogeneic LSCT is limited by the amount of tissue that can be harvested from the donor and by the risk of graft rejection, which is the primary cause of failure in allogeneic LSCT, requiring adequate immunosuppressive therapy to improve long-term survival. Cadaveric allografts offer the advantage of providing a complete limbal tissue for transplantation, thereby providing a larger quantity of stem cells capable of restoring the barrier function of the entire limbus. However, the probability of finding an HLA-compatible cadaveric donor is low, and the quality of donor tissue is unknown.⁽⁹⁾

After allogeneic transplantation, systemic immunosuppression is necessary to prevent immune rejection, observed up to 8 years post-surgery. In many successful cases, no donor DNA is detected in the recipient epithelium, suggesting cessation of immunosuppression. Due to severe ocular complications, keratoprostheses are an alternative to allogeneic LSCT for severe/total bilateral LSCD, as is transplantation of cultivated oral mucosal epithelium.⁽⁹⁾

Systemic immunosuppressive therapy generally includes one or more of the following drugs: corticosteroids (short-term), tacrolimus or cyclosporine, mycophenolate mofetil, or azathioprine.^(4,11,16) Analysis of studies by Le et al.⁽¹¹⁾ shows that patients on a 3-drug regimen had a higher success rate (81.2%; 95% of confidence interval [95%CI] 65.0%-91.0%) than those on fewer immunosuppressants (odds ratio [OR] 3.844; 1.6-9.1; $p = 0.002$). However, the number and dose of medications were not associated with the improvement rate; only prolonged use correlated with higher success rates and improvement. Neither the dosage nor the duration of systemic corticosteroid therapy was associated with clinical outcomes.⁽¹¹⁾

Conjunctival limbal allograft and keratolimbal allograft

The living-related conjunctival limbal allograft (lr-CLAL) and keratolimbal allograft (KLAL) are surgical alternatives for patients with bilateral LSCD. The lr-CLAL method offers benefits due to fresh tissue and strong genetic similarity, as it is sourced from a first-degree relative donor with compatibility. In contrast, KLAL uses cadaveric donor tissue, is more accessible, and offers more stem cells due to the possibility of using more tissue for grafting.⁽⁴⁾ There are various surgical options for bilateral LSCD, one of which is the Cincinnati procedure, which combines lr-CLAL with KLAL.⁽⁴⁾

Statistical data analysis

Several criteria have been described to evaluate surgical success in LSCT for LSCD. Some authors base success on anatomical improvements of the ocular surface, while others focus on functional improvement (such as visual acuity) and patient-reported symptoms.⁽¹¹⁾

Conjunctival limbal autograft versus simple limbal epithelial transplantation versus cultivated limbal epithelial transplantation

In a robust systematic review⁽¹⁵⁾ comparing the primary and secondary measures of these autologous procedures, with an average postoperative follow-up of 1.5 years ($\pm 1-7.6$ years), 68.9% (690/1002, 95% CI 65.9%–71.7%) maintained a stable, epithelialized, avascular cornea, and 60.8% (459/755, 95% CI 57.2%–64.3%) of eyes improved by two lines in best-corrected visual acuity. Statistically, in terms of anatomical success ($p=0.0048$) and functional success ($p \leq 0.0001$), SLET and CLAU showed almost identical anatomical success rates; however, functional success rates were slightly higher with CLAU, which was statistically significant ($p=0.27$). Both methods showed significantly better results compared to CLET.

Conjunctival limbal autograft versus conjunctival limbal allograft versus autologous cultivated limbal epithelial transplantation and allogeneic cultivated limbal epithelial transplantation

A meta-analysis⁽¹¹⁾ of 40 studies analyzed 2,202 eyes, with the number of eyes undergoing CLAU, CLAL, CLET-au, and CLET-al being 505, 742, 771, and 184, respectively. The overall success rate of all LSCT techniques was 67.4% (95%CI 62.1%-72.3%). Overall ocular surface improvement was achieved in 74.5% of all eyes, 85.7% after CLAU (95%CI 79.5%-90.3%), 84.7% after CLET-au (95% CI 77.2%-90.0%), 57.8% after CLAL (95%CI 49.0%-66.1%), and 63.2% after CLET-al (95%CI 49.3%-75.2%). CLAU showed a higher rate of improvement in visual acuity (76%) compared to other procedures (CLAL = 52.3%; CLET-au = 56.4%; CLET-al = 43.3%; $p < 0.001$ for all).

Regarding the type of chemical agent, degree of chemical injury, and preoperative stage of LSCD, differences among the three groups were statistically insignificant; however, the time interval between injury and limbal transplantation was significantly longer in the group that underwent CLET.⁽¹¹⁾

DISCUSSION

The management of chemical burns depends on the time elapsed since the injury. Treatment requires medical and

surgical interventions that correlate with the extent of damage for optimal visual rehabilitation. Surgical treatment may be necessary to promote ocular surface healing and restore stability, corneal clarity, and visual acuity.

Limbal stem cell transplantation has proven effective in treating LSCD. Patients with unilateral deficiency can obtain limbal stem cells from the contralateral healthy eye, referred to as autologous transplantation, which demonstrates excellent results. Alternatively, if the patient wishes to avoid surgery on the healthy eye, they can receive heterologous LSCT from compatible HLA-related living donors or cadavers. For severe bilateral LSCD, only heterologous limbal tissue can be used, performed through allogeneic transplantation, with tissue obtained from HLA-compatible living or cadaveric donors.

Along these lines, further analysis supports the evidence that the procedure grafting iPSC-derived corneal epithelial cell sheets (iCEPs) in patients with LSCD may be a good option, given that the study reported positive outcomes and measures of efficacy showed in all treated eyes that the disease stage had improved, corrected distance visual acuity was enhanced, and corneal opacification had diminished. Furthermore, somewhat unexpectedly, human iPSC-derived corneal cell sheets showed no immune rejection at mid-term evaluations.⁽¹⁸⁾

Precise assessment of LSCD is critical for choosing appropriate treatment, and accurately determining the stage of the injury is crucial for evaluating surgical success. The DUA⁽²⁾ classification system for assessing chemical ocular injury severity can predict visual prognosis; however, there was no consensus on a definitive LSCD scale until 2019, when a new severity assessment system for LSCD was established by the Limbal Stem Cell Working Group.⁽⁹⁾

Our review suggests that the main disadvantages of CLAU are its lack of repeatability and the risk of LSCD in the contralateral healthy eye, whereas CLET has risks related to rejection, the need for systemic immunosuppressive therapy, and high costs for establishing and maintaining a stem cell culture laboratory. On the other hand, CLET is still relatively new and promising, with high success rates and repeatability as its most important advantage.

FINAL CONSIDERATIONS

Chemical injuries can have devastating consequences for the ocular surface and surrounding periocular structures. Most patients with mild, moderate, and even severe chemical injuries, although with an unfavorable prognosis, can achieve a stable ocular surface and functional visual acuity with current management strategies.

Findings from this study suggest that LSCT improves and stabilizes the corneal surface with a low rate of severe ocular complications. CLAU may have a higher success rate and fewer complications than CLAL; however, each case should be individually evaluated to establish appropriate treatment based on injury criteria and ocular surface involvement. Additionally, CLET-au is considered the standard treatment for unilateral LSCD but is limited by its high financial cost.

Currently, there is no single treatment for all types of ocular burns. The best therapeutic approach is case-dependent, based on the nature of the offending agent, extent and severity of damage, the patient's healing response, and available resources. Accurate determination of LSCD stage is essential for evaluating surgical success. The most important factors associated with higher surgical success rates were the type of surgery and the interval between injury and surgery.

LIMITATIONS AND PROPOSING FUTURE RESEARCH DIRECTIONS

Despite the advancement of techniques in recent years across various LSCT modalities, limitations in comparing outcomes remain due to the lack of standardized criteria for assessing LSCD. While several criteria are considered in evaluating success across studies, the main goal of LSCT is to mitigate the severity of LSCD. The Limbal Stem Cell Working Group established a staging system to facilitate accurate assessment of surgical success, diagnosis, LSCD staging, and determination of appropriate treatment.

Our findings support the preference for autologous over allogeneic LSCT, but also highlights the limitation and need for further randomized clinical trials using standardized efficacy measures to determine whether one approach is superior. Finally, there is a notable lack of data in the literature concerning LSCT in relation to corneal transplantation, which would be extremely beneficial as it is an effective procedure for the anatomical and visual rehabilitation of eyes with total LSCD.

AUTHORS' CONTRIBUTION

All authors made substantial contributions to the conception, acquisition of data, analysis and interpretation of data; took part in drafting the article and revising it critically for important intellectual content; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and state to be accountable for all aspects of the work.

REFERENCES

- Kate A, Sharma S, Yathish S, Das AV, Malepati N, Donthineni PR, et al. Demographic profile and clinical characteristics of patients presenting with acute ocular burns. *Indian J Ophthalmol.* 2023;71(7):2694-703.
- Dua HS, Ting DSJ, AlSaadi A, Said DG. Chemical eye injury: pathophysiology, assessment and management. *Eye (Lond).* 2020;34(11):2001-19.
- Ballios BG, Weisbrod M, Chan CC, Borovik A, Schiff JR, Tinckam KJ, et al. Systemic immunosuppression in limbal stem cell transplantation: best practices and future challenges. *Can J Ophthalmol.* 2018;53(4):314-23.
- Baradaran-Rafii A, Eslani M, Haq Z, Shirzadeh E, Huvard MJ, Djalilian AR. Current and upcoming therapies for ocular surface chemical injuries. *Ocul Surf.* 2017;15(1):48-64.
- Basu S, Mohan S, Bhalekar S, Singh V, Sangwan V. Simple limbal epithelial transplantation (SLET) in failed cultivated limbal epithelial transplantation (CLET) for unilateral chronic ocular burns. *Br J Ophthalmol.* 2018;102(12):1640-5.
- Basu S, Sureka SP, Shanbhag SS, Kethiri AR, Singh V, Sangwan VS. Simple limbal epithelial transplantation: long-term clinical outcomes in 125 cases of unilateral chronic ocular surface burns. *Ophthalmology.* 2016;123(5):1000-10.
- Borroni D, Wowra B, Romano V, Boyadzhieva M, Ponzin D, Ferrari S, et al. Simple limbal epithelial transplantation: a review on current approach and future directions. *Surv Ophthalmol.* 2018;63(6):869-74.
- Campbell JD, Ahmad S, Agrawal A, Bienek C, Atkinson A, McGowan NW, et al. Allogeneic Ex Vivo Expanded Corneal Epithelial Stem Cell Transplantation: A Randomized Controlled Clinical Trial. *Stem Cells Transl Med.* 2019;8(4):323-31.
- Deng SX, Kruse F, Gomes JA, Chan CC, Daya S, Dana R, et al. Global consensus on the management of limbal stem cell deficiency. *Cornea.* 2020;39(10):1291-302.
- Korkmaz I, Palamar M, Egrilmez S, Gurdal M, Yagci A, Barut Selver O. Evaluation of Limbal Stem Cell Transplant Success in Ocular Chemical Injury. *Exp Clin Transplant.* 2023;21(8):684-90.
- Le Q, Chauhan T, Yung M, Tseng CH, Deng SX. Outcomes of limbal stem cell transplant: a meta-analysis. *JAMA Ophthalmol.* 2020;138(6):660-70.
- Ramírez BE, Sánchez A, Herreras JM, Fernández I, García-Sancho J, Nieto-Miguel T, et al. Stem cell therapy for corneal epithelium regeneration following good manufacturing and clinical procedures. *Biomed Res Int.* 2015;2015:408495.
- Sangwan VS, Basu S, Vemuganti GK, Sejal K, Subramaniam SV, Bandyopadhyay S, et al. Clinical outcomes of xeno-free autologous cultivated limbal epithelial transplantation: a 10-year study. *Br J Ophthalmol.* 2011;95(11):1525-9.
- Sangwan VS, Basu S, MacNeil S, Balasubramanian D. Simple limbal epithelial transplantation (SLET): a novel surgical technique for the treatment of unilateral limbal stem cell deficiency. *Br J Ophthalmol.* 2012;96(7):931-4.
- Shanbhag SS, Nikpoor N, Rao Donthineni P, Singh V, Chodosh J, Basu S. Autologous limbal stem cell transplantation: a systematic review of clinical outcomes with different surgical techniques. *Br J Ophthalmol.* 2020;104(2):247-53.
- Shanbhag SS, Saeed HN, Paschalis EI, Chodosh J. Keratolimbal allograft for limbal stem cell deficiency after severe corneal chemical injury: a systematic review. *Br J Ophthalmol.* 2018;102(8):1114-21.
- Vazirani J, Basu S, Kenia H, Ali MH, Kacham S, Mariappan I, et al. Unilateral partial limbal stem cell deficiency: contralateral versus ipsilateral autologous cultivated limbal epithelial transplantation. *Am J Ophthalmol.* 2014;157(3):584-90.e1-2.
- Soma T, Oie Y, Takayanagi H, Matsubara S, Yamada T, Nomura M, et al. Induced pluripotent stem-cell-derived corneal epithelium for transplant surgery: a single-arm, open-label, first-in-human interventional study in Japan. *Lancet.* 2024;404(10466):1929-39.