A systematic literature review of surgical interventions for limbal stem cell deficiency in humans

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CRD summary
The authors concluded that there was insufficient evidence to determine the optimal surgical technique for patients with limbal stem cell deficiency and a multicentre register was required. There were limitations to the review, but overall the authors' conclusions reflected limited evidence from poor quality diverse observational studies and were likely to be reliable.

Authors' objectives
To evaluate the benefits and harms of surgical interventions for limbal stem cell deficiency (LSCD).

Searching
MEDLINE, EMBASE, Science Citation Index, BIOSIS Previews and the Cochrane Library were searched from 1989 to September 2006. Search terms were reported. Only English language reports were eligible. In addition, reference lists were screened. Conference abstracts were excluded.

Study selection
Randomised controlled trials (RCTs), non-randomised comparative studies and case series with at least 15 eyes that evaluated surgical interventions for LSCD were eligible for inclusion. Studies that evaluated keratoprosthesis were excluded. The diagnosis of LSCD was expected to be confirmed by impression cytologic analysis in addition to clinical impression (it was not clear if this was a requirement for inclusion). The primary review outcome was an improvement in vision of at least two Snellen lines of best-corrected visual acuity (BCVA). The review also assessed adverse events. Secondary outcomes were ocular comfort and restoration of corneal epithelial phenotype.

The included studies evaluated a variety of surgical interventions and often combinations of different interventions. The most commonly used interventions included keratolimbal allograft (KLAL), penetrating keratoplasty (PK), conjunctival-limbal autograft (CLAU), amniotic membrane transplantation (AMT), deep lamellar keratoplasty (DLK) and cataract surgery; some interventions were combined with systematic immunosuppression. Indications for surgery included bilateral and unilateral severe and partial LSCD due to chemical and thermal burns, aniridia and Stevens-Johnson syndrome. The mean duration of follow-up ranged from 6.8 to 60 months where reported.

One reviewer screened titles and abstracts.

Assessment of study quality
Two masked reviewers independently assessed validity using a checklist developed by the Review Body for Interventional Procedures. Discrepancies were resolved by consensus with the aid of a third reviewer if required. Criteria included representative sample, consecutive enrolment, clear recruitment period, objective outcome measures, clarity of reporting of main findings, follow-up more than three years, prospective data collection, recording of prognostic factors and reporting of drop-outs.

Data extraction
Two reviewers independently extracted data on clinical outcomes and adverse events. Where possible, the number of patients with improved VA from baseline was presented for each study.

Methods of synthesis
The studies were grouped by the type and severity of limbal stem cell deficiency and combined in narrative synthesis.

Results of the review
Twenty-six noncomparative case series were included (n=687 patients and 738 eyes).
Most studies evaluated a representative sample, assessed objective outcome measures and clearly reported main findings. Flaws included non-consecutive selection, follow-up less than three years, patients entered at different stages of disease, retrospective data collection, failure to identify all prognostic factors and no information about drop-outs.

Bilateral severe or total limbal stem cell deficiency: The most common surgical procedure was keratolimbal allograft plus systematic immunosuppression. An improvement on BCVA of two lines or more was reported in 31 per cent to 67 per cent of eyes (three studies). A reduction in VA from baseline was reported in zero to 18 per cent of patients. Other adverse events included postoperative glaucoma (26 per cent to 32 per cent across three studies), microbial keratitis (eight per cent to 14 per cent across two studies) and corneal necrosis (14 per cent in one study).

Unilateral severe total limbal stem cell deficiency: The most common surgical procedure was contralateral conjunctival limbal autograft. An improvement on BCVA of two lines or more was reported in 35 per cent to 88 per cent of eyes (five or eight studies, the number of studies providing data was not entirely clear). Adverse events in patients who had undergone CLAU procedures (with or without other procedures) included a reduction in VA from baseline in zero to four per cent of patients and postoperative glaucoma in zero to nine per cent. For patients who had undergone KLAL, a reduction in VA from baseline was reported in zero to nine per cent and glaucoma in 19 to 37 per cent.

Partial limbal stem cell deficiency: The only study in patients with partial LSCD evaluated AMT and reported an improvement on BCVA of two lines or more in 59 per cent of patients (10/17; reported as 39 per cent in the abstract). One patient (six per cent) had a reduction in VA and one had an immune rejection episode.

Results for other studies were also reported.

Authors’ conclusions
There was insufficient evidence to determine the optimal surgical technique for patients with LSCD. There was a need for a multicentre LSCD register to standardise data collection.

CRD commentary
The review question was clearly stated and inclusion criteria were specified; criteria for intervention and study design were broad. Several relevant sources were searched, but no attempts were made to minimise publication or language bias. Appropriate methods were used to minimise reviewer error and bias during the review process. Methods were used to minimise reviewer errors and bias in the assessment of validity and extraction of data, but similar methods were not used for study selection. Validity was assessed and results were reported. In view of the diversity among studies a narrative synthesis was appropriate. There were limitations to the review. Overall the authors’ conclusions reflected limited evidence from poor quality diverse observational studies and were likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that if an RCT was not feasible then a multicentre LSCD register should be developed to allow standardised data collection for patients with LSCD. Data should include methods used to diagnose LSCD, prognostic factors, preoperative VA, full reporting of all procedures and co-interventions, postoperative corneal phenotype with impression cytologic results, postoperative VA, patient comfort and adverse events.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.