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NHS
National Institute for Health and Clinical Excellence

Tissue-cultured limbal stem cell allograft transplantation for regrowth of corneal epithelium

1 Guidance

1.1 Current evidence on the safety and efficacy of tissue-cultured limbal stem cell allograft transplantation for regrowth of corneal epithelium does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research.

1.2 Clinicians wishing to use tissue-cultured limbal stem cell allograft transplantation for regrowth of corneal epithelium should take the following actions.

- Inform the clinical governance leads in their Trusts.
- Ensure that patients understand the uncertainty about the procedure's safety and efficacy, and provide them with clear written information. In addition, use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG216publicinfo).
- Audit and review clinical outcomes of all patients having tissue-cultured limbal stem cell allograft transplantation for regrowth of corneal epithelium (see section 3.1).

1.3 Further research on long-term outcomes and the risks and benefits of long-term systemic immunosuppressant regimes would be useful. The Institute may review the procedure upon publication of further evidence.

2 The procedure

2.1 Indications

2.1.1 The procedure is used to treat limbal stem cell deficiency (LSCD). The limbus is the part of the eye where the cornea joins the sclera, and where the conjunctiva, which covers the sclera, ends. Undifferentiated epithelial cells are produced at the limbus and differentiate to become corneal epithelial cells. Failure of this process can result in a variety of serious and intractable disorders of the ocular surface, including loss of corneal transparency which impairs vision. Limbal stem cells may be damaged by various disease processes or chemical injury.

2.1.2 The aim of treatment is to restore a healthy conjunctival and corneal surface. Simple treatments include topical steroids, ocular lubricants, bandage contact lenses and autologous serum. Patients with more serious LSCD may require surgical procedures such as conjunctival and keratolimbal allografts, possibly followed by corneal grafts. For patients with unilateral LSCD, the use of limbal stem cells from the fellow eye may be enhanced by tissue culture prior to grafting.

2.2 Outline of the procedure

2.2.1 Stem cells for allograft transplantation are harvested from the limbal corneal tissue of donor eyes (from either matched living relatives or cadaveric donors). The donor stem cells are obtained by excising a small area of the conjunctiva at the limbus, which is a minor procedure for the living donor. The tissue obtained is grown in culture and, once the cells have multiplied sufficiently, small sheets of cells, supported by an amniotic membrane or plastic, are transplanted onto the affected eye(s). The surgery is performed under local or general anaesthesia. A protective soft contact lens may be applied, and the eye is kept moist with artificial tears in the period immediately after surgery. The procedure can be repeated if necessary.

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This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Interventional procedures guidance is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland.

This guidance is endorsed by NHS QIS for implementation by NHSScotland.

NHS Quality Improvement Scotland

2.2.2 Systemic immunosuppressants are required to minimise the risk of graft rejection. The duration, type and dose of immunosuppressants vary and long-term use may be necessary.

2.3 Efficacy

2.3.1 Most studies reported efficacy outcomes relating to resolution of LSCD in terms of corneal re-epithelialisation and/or resolution of corneal vascularisation, corneal conjunctivilisation, inflammation/scarring, pain, photophobia and corneal opacity. Definitions of success varied between studies. Resolution of LSCD was achieved following tissue-cultured limbal stem cell transplantation in between 70% (7/10) and 100% (4/4, 7/7 and 13/13) of eyes.

2.3.2 In one case series, complete epithelialisation of the corneal surface was achieved in 80% (8/10) of eyes by the time the amniotic membrane had dispersed. In another series, corneal epithelialisation was achieved in 46% (6/13) of eyes at final follow-up (length of follow-up not stated). In a case series of 10 patients, corneal epithelialisation was incomplete; corneal epithelial defects (one of them persistent) were reported in 2 patients. In another case series of seven patients there were two transient epithelial defects which resolved after 2–3 weeks with topical antibiotic treatment.

2.3.3 The case series reported visual acuity following tissue-cultured limbal stem cell allograft transplantation in 40% (4/10), 77% (10/13) and 100% (7/7) of eyes, although concomitant surgery to improve vision was undertaken in some patients. For more details, refer to the 'Sources of evidence' section.

2.3.4 The Specialist Advisers stated that if the graft works well, the procedure is highly effective in producing visual benefit.

2.4 Safety

2.4.1 Bacterial infection following tissue-cultured limbal stem cell allograft transplantation occurred in 8% (1/13),15% (2/13) and 25% (1/4) of eyes. In one case series, corneal perforation occurred in 31% (4/13) of eyes.

2.4.2 Post-procedural development of glaucoma requiring trabeculotomy was reported in 8% (1/13) of eyes in one case series (follow-up not stated). One case series of seven patients with between 6 and 20 months follow up reported no significant postoperative complications. For more details, refer to the 'Sources of evidence' section.

2.4.3 The Specialist Advisers stated that theoretical risks include transmission of infection by donor tissue and rejection of the graft. They also raised the theoretical possibility of subsequent limbal stem cell failure in the donor, requiring treatment at a later date.

3 Further information

3.1 This guidance requires that clinicians undertaking the procedure make special arrangements for audit. The Institute has identified relevant audit criteria and developed an audit tool (which is for use at local discretion) available from www.nice.org.uk/IPG216

Andrew Dillon
Chief Executive
April 2007

Information for patients

The Institute has produced information describing its guidance on this procedure for patients, carers and those with a wider interest in healthcare. It explains the nature of the procedure and the decision made, and has been written with patient consent in mind. This information is available from www.nice.org.uk/IPG216publicinfo

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the following document.

'Interventional procedure overview of tissue-cultured limbal stem cell allograft transplantation for regrowth of corneal epithelium', September 2006.

Available from: www.nice.org.uk/ip350overview

Ordering information
Copies of this guidance can be obtained from the NHS Response Line by telephoning 0870 1555 455 and quoting reference number N1239. 'Understanding NICE guidance' can be obtained by quoting reference number N1240.

The distribution list for this guidance is available at www.nice.org.uk/IPG216distributionlist

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