NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes

The cornea is the clear outer layer at the front of the eyeball that acts as a window to the eye. Injury, surgery or disease can make the cornea cloudy, affecting vision.

A corneal graft–keratoprosthesis is an artificial cornea surrounded by a corneal graft from a human donor. It is implanted to replace a severely diseased cornea in wet eyes with good blinking function.

The National Institute for Health and Care Excellence (NICE) is examining implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.
- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the Interventional Procedures Programme process guide, which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 6th August 2015

Target date for publication of guidance: October 2015

1 Provisional recommendations

1.1 Current evidence on the efficacy of implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes is adequate in the short to medium term. Although the evidence on safety shows a high incidence of significant adverse effects, there are few options for patients with severe corneal opacity if standard corneal grafts have failed or are not appropriate. Therefore this

procedure may be used with normal arrangements for clinical governance, consent and audit.

1.2 During the consent process, clinicians should ensure that patients understand the balance of risks and benefits of this procedure, including: the need for long-term follow-up, which some patients find burdensome; the possibility that sight may not improve and may deteriorate; and the risk of serious complications. Patients should be provided with clear information in an appropriate format. In addition, the use of NICE's information for the public [[URL to be added at publication]] is recommended.

1.3 Implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes should only be done on carefully selected patients with corneal blindness, when standard treatments such as keratoplasty have failed or are not appropriate.

1.4 Implantation of a corneal graft–keratoprosthesis for severe corneal opacity in wet blinking eyes should only be done in specialist centres by surgeons experienced in the technique; long-term follow-up should be carried out by an experienced multidisciplinary team.

2 Indications and current treatments

2.1 Injury or disease of the cornea can make it opaque, stopping light from entering the eye and resulting in loss of vision. Corneal injuries can be caused by direct trauma, including surgery, as well as chemical or thermal burns. Diseases that can cause corneal opacity include autoimmune diseases, bullous keratopathy, keratoconus, keratitis and corneal stromal dystrophies.

2.2 The standard treatment for significant corneal opacity is a corneal transplant (penetrating keratoplasty). Penetrating keratoplasty removes the opaque cornea using a trephine, replacing it with a donor cornea. Some patients cannot have a standard corneal transplant for reasons including: disease severity; severe involvement of the conjunctiva; a failed previous corneal transplant; or when measures needed to prevent graft rejection are contraindicated. For these patients, penetrating keratoplasty using an artificial cornea (keratoprosthesis) may be an option.

3 The procedure

3.1 A corneal graft–keratoprosthesis is an artificial clear central corneal window surrounded by a human donor cornea. Implantation is generally done if a standard corneal transplant has failed, or when it is inappropriate. The procedure is used to treat only the most severe corneal opacity.

3.2 A type I corneal graft–keratoprosthesis is the most commonly implanted artificial corneal device and is suitable for wet blinking eyes that have had multiple graft failures. It is custom-made to have a range of dioptric powers to match the axial length of the patient's aphakic eye and is shaped like a collar button, with a refractive front and porous back plate and a titanium locking ring.

3.3 Implantation of the fully assembled corneal graft–keratoprosthesis is done under general or local anaesthesia. A human donor corneal graft with a central hole is positioned between the front and back plate, and held in place by the titanium ring. The central portion of the patient's opaque cornea is removed and if the natural lens is in place, it is also removed. The corneal graft–keratoprosthesis is then transferred to the patient's corneal opening and secured with

multiple interrupted sutures. Finally, a soft bandage contact lens is placed on the surface of the eye.

3.4 Postoperatively, patients wear a soft contact lens and use prophylactic antibiotic drops for the rest of their lives. In addition, topical steroids are usually recommended and patients need frequent follow-up and monitoring for life.

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview ***[add URL]***.

4.1 A case series of 150 patients (158 eyes) who had type I corneal graft–keratoprosthesis implantation reported that preoperatively only 9% of eyes had best corrected visual acuity (BCVA) of 20/200 or better. Postoperatively, 70% (97/138) of eyes had achieved BCVA of 20/200 or better at a median follow-up of 6.3 months; 30% (41/138) of eyes did not achieve BCVA of 20/200 or better because of pre-existing posterior segment conditions. The probability of maintaining the same vision at 7 years (n=97 eyes; estimated with Kaplan–Meier survival curves) was 50%.

4.2 The case series of 150 patients (158 eyes) reported an overall device retention rate of 84% at 2 years and 67% (89/133) at 7-year follow-up.

4.3 The case series of 150 patients (158 eyes) reported device removal in 33.2% (44/133) of patients at 7-year follow-up. In 25% (35/139) of eyes, the device was removed (30/139) or the eye was

enucleated (5/139) as a result of device-related complications during follow-up.

4.4 The case series of 150 patients (158 eyes) reported that 11.9% (5/42) of eyes had repeated keratoprosthesis implantation because of recurrent corneal melts with device extrusion.

4.5 A case series of 24 patients who had corneal graft–keratoprosthesis implantation (type I in 23 patients and type II in 1 patient) reported significant improvement in postoperative vision-related quality of life (assessed using the National Eye Institute Visual Functioning Questionnaire [NEI VFQ-25]) at 3-month follow-up when compared with baseline scores (patient-reported visual function overall score: 43.1 versus 70.0 [$p<0.001$]). Subscale scores within NEI VFQ-25 showed significant improvement in general vision, near and distance activities, social functioning, mental health, role difficulties, dependency, colour vision and peripheral vision ($p<0.05$). The improvement was also seen when comparing baseline scores with postoperative scores at an average follow-up of 16 months.

4.6 The specialist advisers listed key efficacy outcomes as improvement in visual acuity, adequate management of glaucoma and device retention.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

5.1 Retroprosthetic membrane formation was reported in 54% (22/41) of eyes in a case series of 37 patients who had type I corneal graft–keratoprosthesis implantation at a mean follow-up of 22 months. Fourteen patients needed treatment with yttrium-aluminium-garnet (YAG) laser (3 of them needed additional surgical membranectomy) and 8 patients did not need any treatment. In 6 patients, retroprosthetic membrane formation was secondary to concomitant surgical procedures. Epiretinal membrane formation was reported in 1 patient in a case series of 40 patients (42 eyes) at 1-year follow-up (further details were not reported).

5.2 Corneal melting was reported in 24% (10/42) of eyes in the case series of 40 patients at a mean follow-up of 64 months. This occurred in patients with Stevens–Johnson syndrome and the melt led to further morbidity, infection and implant extrusion.

5.3 Chorioretinal adhesion problems (retinal detachment with or without choroidal detachment or retinoschisis) were reported in 27% (11/41) of eyes in a case series of 37 patients at a mean follow-up of 22 months. Six patients needed surgery: 5 had vitrectomy and 1 had trans-scleral cyclophotocoagulation.

5.4 Glaucoma or increased intraocular pressure was reported in 81% (34/42) of eyes (5 with, and 29 without, Stevens–Johnson syndrome) in the case series of 40 patients at a mean follow-up of 64 months. Increased intraocular pressure was noted in 19% (8/42) of eyes, glaucoma was newly diagnosed in 30% (13/42) of eyes and 30% (13/42) of eyes with preoperative glaucoma had disease progression. All were treated with anti-glaucoma drugs (mean 2.7 drugs per eye), but 12 needed surgical interventions at a mean

follow-up of 22.1 months, corresponding to a glaucoma surgery rate of 0.062/eye year.

5.5 Infectious endophthalmitis was reported in 16% (20/133) of patients in the case series of 150 patients (158 eyes) at 7-year follow-up (further details were not reported). Infectious keratitis was reported in 21% (9/42) of eyes (3 with autoimmune disease and 6 with non-autoimmune disease) in the case series of 40 patients at a mean follow-up of 64 months (further details were not reported).

5.6 Sterile corneal necrosis was reported in 20% (26/133) of patients in the case series of 150 patients (158 eyes) at 7-year follow-up (further details were not reported).

5.7 Sterile vitritis was reported in 4% (4/101) of eyes in an international series and 11% (10/94) of eyes in a US series in a retrospective case series of 194 patients at a mean follow-up of 14.2 and 24.1 months (further details were not reported).

5.8 Cystoid macular oedema was reported in 10% (13/133) of patients in the case series of 150 patients (158 eyes) at 7-year follow-up (further details were not reported).

5.9 Persistent epithelial defects were reported in 10% (10/101) of eyes in the international series and 36% (34/94) of eyes in the US series in the retrospective case series of 194 patients at a mean follow-up of 14.2 and 24.1 months (further details were not reported).

5.10 Vitreous haemorrhage was reported in 10% (4/42) of eyes in the case series of 40 patients at 1-year follow-up (further details were not reported). Choroidal haemorrhage was reported in 3% (4/122)

of patients in the case series of 122 patients (126 eyes) at 6-month follow-up (further details were not reported).

5.11 Device leaks at the keratoprosthesis stem (through the cornea-anterior front plate interface of the device) were reported in 3 eyes (at a mean of 13.7 months) after type I corneal graft-keratoprosthesis implantation in a case report of 3 patients. In 1 patient, the leak was not evident; in the second patient, a repeat keratoprosthesis implantation was needed to stop the persistent leak; in the third patient the persistent leak was repaired with glue.

5.12 Traumatic wound rupture (at the graft–host junction) at an average of 4.2 months after type I corneal graft–keratoprosthesis implantation was reported in 3% (4/136) of eyes in a case series of 122 patients. In 2 eyes, the device was extruded and therapeutic penetrating keratoplasties were performed, but vision deteriorated. In 2 eyes with wound rupture, suturing of the wound was done. Vision improved in 1 eye and in the other it was stable.

5.13 Occlusive vasculopathy (peripheral occlusive vasculitis and ischaemia of the entire retina) was reported in 5% (2/41) of eyes in the case series of 37 patients at a mean follow-up of 22 months (further details were not reported).

5.14 Corneal infiltrate was reported in 12% (12/101) of eyes in the international series and 10% (9/94) of eyes in the US series in the retrospective case series of 194 patients at a mean follow-up of 14.2 and 24.1 months (further details were not reported).

5.15 Scleritis was reported in 1 patient in a case series of 122 patients (126 eyes) at 6-month follow-up (further details were not reported).

5.16 Chronic hypotony was reported in 9% (6/67) of patients in a case series of 68 patients at a median follow-up of 18.5 months after type I corneal graft–keratoprosthesis implantation. The incidence of chronic hypotony was 3.7% at 1 year (95% confidence interval [CI] 0.9% to 14%) and 13.3% at 2 years (95% CI 5.5% to 30%). All eyes had retroprosthetic membranes and decreased visual acuity and 5 eyes had previous history of glaucoma or ocular hypertension. Four patients had pars plana vitrectomy and silicone oil injection and reported increased vision ranging from 'hand motion' to 20/400. One patient with 1 affected eye deferred treatment and the eye progressed to phthisis bulbi needing enucleation. One eye had pre-phthisis and no surgery was needed.

5.17 Posterior capsular tear was reported in 1 patient during the surgery in the case series of 40 patients (further details were not reported).

5.18 Sterile corneal ulceration at the graft–optic junction was reported in 22% (2/9) of eyes (1 after 52 months and 1 at 10 months), in a case series of 9 patients (9 eyes) with failed interventions for chemical and thermal injury. Both devices were removed and replaced, 1 also had a concomitant retinal detachment repair. Vision deteriorated in 1 eye and the other eye developed endophthalmitis and became blind and painful, and was enucleated.

5.19 Horizontal diplopia after type I corneal graft-keratoprosthesis implantation was reported in a patient with a history of trauma and a series of failed corneal transplants. Strabismus surgery restored binocular vision.

5.20 Pigmented deposit on the keratoprosthesis (a large central black deposit on the bandage contact lens on the front plate of the

device) associated with the use of topical ibopamine as a treatment for chronic hypotony was reported in a patient implanted with a type I device. Postoperatively, vision improved to a best corrected visual acuity (BCVA) of 20/200, but after 3 months, vision deteriorated because of the pigmented deposit. This was treated by removing the bandage contact lens and changing to a daily disposable contact lens and regular cleaning of the front plate with diluted baby shampoo and surgical sponges.

5.21 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers reported no anecdotal or theoretical adverse events.

6 Committee comments

6.1 The Committee noted the high level of complications documented in the literature, including permanent loss of sight. However, the Committee was aware that for patients with severe corneal disease causing blindness, who have few alternative options, this procedure could mean regaining some vision for a period of time. The Committee also noted that this procedure is only normally offered after a failed standard corneal graft.

6.2 The Committee was advised that the procedure should not be done in patients who have adequate vision in 1 eye.

7 Further information

7.1 For related NICE guidance, see the NICE website.

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