Epikeratophakia Grafts Glued with Autologous Cryoprecipitate

CHAD K. ROSTRON

Department of Ophthalmology, Leicester Royal Infirmary, Leicester LE1 5WW, England

This study set out to determine if adhesive could be used instead of sutures for fixing epikeratophakia lenticules in place. Three patients who had previously undergone removal of a traumatic cataract, and who were contact lens intolerant, each had a specially designed lyophilized epikeratophakia graft glued onto their aphakic eye. Adhesive was prepared by separation of cryoprecipitate from plasma derived individually from each patient. The cryoprecipitate was used to form a fibrin bond beneath the graft by the addition of topical thrombin. All the grafts were successfully retained and rapidly re-epithelialized, and in a 6-month follow-up period no complications attributable to the use of adhesive were encountered. These preliminary results suggest that gluing epikeratophakia grafts significantly improves the procedure by making it quicker, easier and potentially more effective.

Keywords: Epikeratophakia grafts; Adhesive; Cryoprecipitate

INTRODUCTION

An epikeratophakia lenticule is normally secured in place with multiple interrupted monofilament sutures. Not only is this procedure time consuming, but also technically exacting, since if the suture tension is incorrect the accuracy of refractive correction may be impaired [1]. Various attempts have therefore been made to dispense with the need for sutures in epikeratophakia. Keates and co-workers attempted to weld grafts in place with a carbon dioxide laser, but was unsuccessful [2]. Robin used a mollusc-derived adhesive, but additional sutures were still necessary initially to stabilize the graft [3].

However, recent experimental work using Tisseel (Immuno Ag, Vienna, Austria), a commercially prepared fibrinogen adhesive, to glue experimental epikeratophakia grafts has been successful [4]. Tisseel adhesive is a lyophilized cryoprecipitate prepared from pooled donated human plasma, and although the product is heat treated to diminish the risk of transmission of viral disease, it is not currently licensed for clinical use in the UK. Because of this, further experiments were carried out to prepare fibrinogen adhesive from *single donors* and this also proved effective in gluing experimental epikeratophakia grafts in rabbits [5]. The technique of using autologously prepared cryoprecipitate to fix epikeratophakia grafts has now been successfully used in the clinical situation and is the subject of this paper.

Correspondence to: Mr C.K. Rostron, Consultant Ophthalmologist, Department of Ophthalmology, St. George's Hospital, Blackshaw Road, London SW17 0QT.

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PATIENTS AND METHODS

Patients

The 3 patients in this study had suffered from penetrating corneal injury complicated by cataract formation. Cataract extraction had been carried out between 4 and 10 years previously, and contact lens wear subsequently attempted. All patients were unable to tolerate daily-wear contact lenses and had been considered unsuitable for secondary intraocular lens implantation due to their young age (27–37 years), and to the risks associated with further intraocular surgery. All the patients were highly hypermetropic in their aphakic eyes, with unaided visual acuities of 'counting fingers' only.

Adhesive preparation

Fibrinogen adhesive was prepared from each patient by obtaining 45 ml of blood into a syringe containing

5 ml of 3.8% w/v sodium citrate. The blood was centrifuged and the plasma separated and frozen to −79 °C. This was then allowed to thaw to 4 °C overnight. The precipitated fibrinogen was separated out by further centrifugation at 4 °C and the supernatant serum discarded. The cryoprecipitate was then refrozen to −79 °C and stored for up to 1 week.

Lenticule Preparation

Corneal tissue was obtained from donors who were sero-negative for evidence of infection with human immunodeficiency virus or hepatitis B. The tissue used was unsuitable for penetrating keratoplasty due to poor endothelial cell count. The corneas were stored in cryoprotective solution in liquid nitrogen for periods of up to 3 months.

The lenticules were prepared in our own laboratory by lathing the corneal tissue in a desiccated state at room temperature [1, 6]. Discs of 9 mm diameter were punched from the corneoscleral segments and desiccated at 4 °C for 48 h. The corneal discs were lathed with a diamond tool at speed of 6000 rev/min. The lenticules were cut with various optic zone parameters as part of a current study into the factors affecting refractive outcome in epikeratophakia. After lathing, the lenticules were freeze-dried for 24 h at 3 mbar pressure, and −50 °C. They were then stored under vacuum at room temperature for periods of up to 1 month.

Surgical Technique

A circular mark of 6 mm diameter was made on the patient's cornea, centred around the visual axis. The epithelium was stripped within the mark only, and a very shallow cut made in the superficial stroma with a diamond knife. A broad lamellar dissection was made, extending outwards about 2 mm from the circular keratotomy. The cryoprecipitate was warmed to room temperature, becoming a moderately viscous fluid, of which 2 drops were applied to the cornea and spread into the lamellar split. The rehydrated lenticule was then placed in position and its wing zone tucked beneath the surface of the recipient cornea (Fig. 1). Bovine thrombin (Thrombinar: Armour Pharmaceuticals, Illinois, USA) 500 IU/litre in a solution of calcium chloride 40 mmol/litre was applied externally and the graft monitored until coagulation of the glue was apparent (1–2 min). The lids were secured with a temporary tarsorrhaphy suture to expedite re-epithelialization [7].

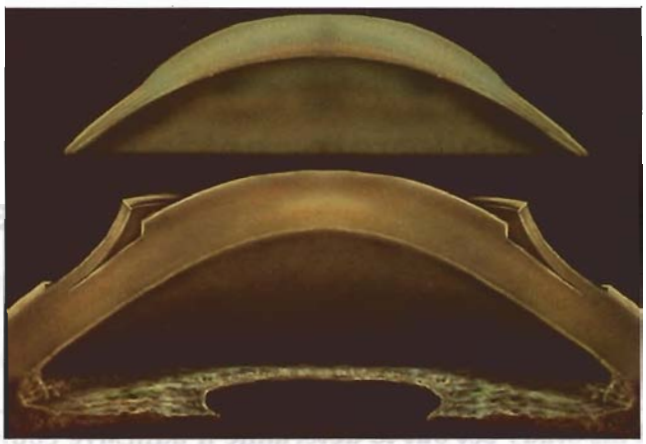

Fig. 1 The lenticule has a broad and thin wing zone to tuck into the broad lamellar split in the host stroma

RESULTS

All 3 patients in this series successfully retained their epikeratophakia grafts and no complications attributable to the use of adhesive occurred during the 6 months' follow-up.

Patient 1

This patient's graft had re-epithelialized by the fourth postoperative day and the tasorrhaphy suture was opened at this time. On examination it was found that a residual strand of fibrin was adherent to the cornea at the site of the graft–host junction (Fig. 2). This fibrin strand was removed under topical anaesthesia without disturbing the surrounding epithelium. At 1 month postoperatively the graft and graft–host interface were clear, and visual acuity corrected to 6/24 with a −3.5 dioptre (D) sphere. When last seen at 6 months postoperatively, the visual acuity was 6/12 unaided, correcting to 6/6 with +0.75 D Sph./+2.0 D Cyl × 90°. The change in corneal contour brought about by the surgery is shown by photokeratoscopy in Figs 3(a) and 3(b).

Patient 2

This patient's original perforating corneal injury had caused fairly extensive corneal scarring and irregularity. At the time of graft surgery it was noted that there was some unevenness in the surface of the lenticule in the area overlying the scar on the patient's cornea. The graft re-epithelialized in 4 days. When seen last at follow-up at 5 weeks postoperatively, visual acuity was 6/60 unaided, 6/12 with a pinhole. Photokeratoscopy showed distortion of the lenticule surface in the area over the pre-existing scar and it was thought that the resultant irregular

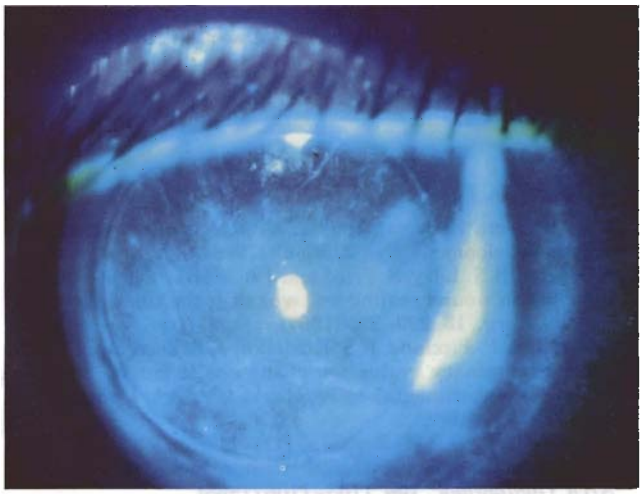

Fig. 2 Epikeratophakia graft 4 days postoperatively stained with fluorescein and viewed under cobalt blue light. The epithelium is intact and a strand of fibrin glue covered with mucus is seen at the graft–host junction.

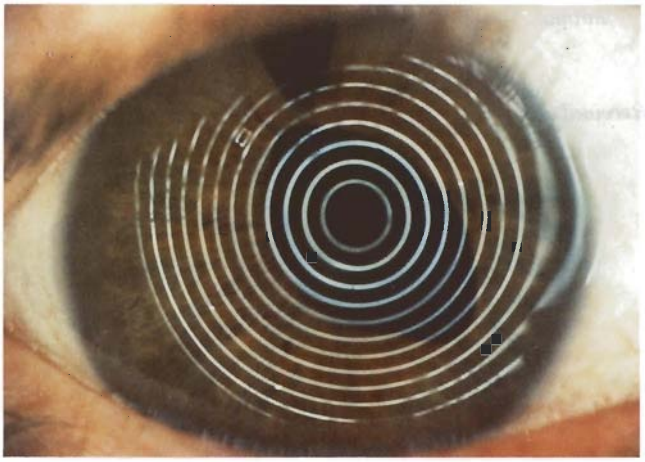

Fig. 3(a) Photokeratograph of patient 1 preoperatively

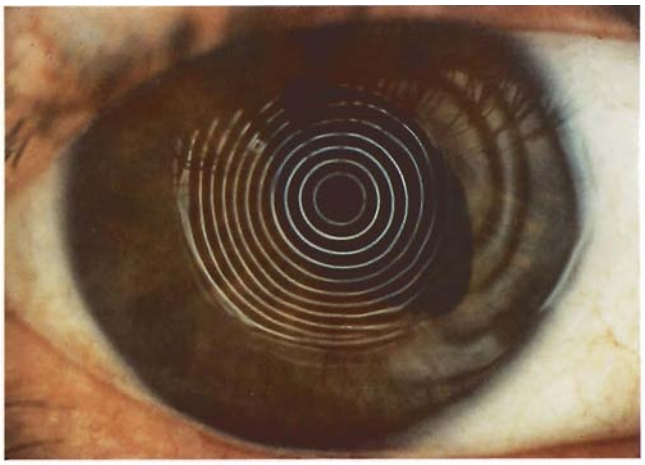

Fig. 3(b) Photokeratograph of patient 1, 6 weeks after glued epikeratophakia graft

astigmatism accounted for the relatively poor acuity at this early postoperative stage.

Patient 3

This patient's tarsorrhaphy was opened 3 days postoperatively, and the graft had re-epithelialized in 5 days. When last seen at 1 month postoperatively, visual acuity was 6/36 with −1.5 D sphere and N8 unaided and the graft and graft–host interface were clear (Fig. 4).

Fig. 4 Glued epikeratophakia graft 1 month postoperatively (patient 3). The graft is clear, but a scar in the host cornea from the original perforating injury is visible beneath the lenticule

DISCUSSION

Previous experimental work has shown that by using a large diameter graft in a small diameter bed a proportion of epikeratophakia grafts can be retained without either sutures or adhesives [4], and that the use of fibrin adhesive increased the proportion of grafts retained. These findings suggested that the adhesive technique could be effective in the clinical situation. None of the grafts in this preliminary series was lost and the stability of the grafts was satisfactory from the time of completion of surgery. All of the grafts re-epithelialized readily and it seems likely that the absence of sutures allowed stabilization of the epithelium to occur more quickly than if sutures had been present. Although excess fibrin was seen on the graft surface of one patient's eye (Fig. 2), this did not appear to have inhibited re-epithelialization. In the other cases it was not possible to detect the presence of the glue at postoperative clinical examination, and autologously derived fibrinogen seems to behave in a manner similar to that of commercial pooled donor fibrinogen adhesive.

By gluing the graft the surgical procedure is consi-

derably simplified, taking typically only half the time required for a sutured graft. This makes it easier to operate under local anaesthesia in those unfit or unwilling to have a general anaesthetic. In addition, paediatric patients undergoing epikeratophakia could avoid the second anaesthetic which would otherwise be needed to remove the sutures. The possibility that the use of adhesive reduces the scope for unpredictable variation of corneal contour induced by suturing, and could therefore enhance the accuracy of refractive correction, needs to be demonstrated by a comparative trial of the two techniques.

CONCLUSION

The preliminary results of a trial of autologous cryoprecipitate used as the sole agent to fix epikeratophakia grafts has shown promising results. Further studies and follow-up are necessary to compare this technique with the standard method using sutures.

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