PostScript

LETTERS

The use of fibrin adhesive in trabeculectomy: a pilot study

During trabeculectomy, tight suturing of the scleral flap to avoid overfiltration may pose a risk of increased intraocular pressure (IOP) and a flat non-functioning bleb. Furthermore, the nylon sutures usually used to reattach the conjunctiva to the limbus may tear out of the conjunctiva and induce an inflammatory reaction. To overcome these problems, investigators have suggested the use of laser suture lysis¹ or releasable sutures² or other types of closure methods, such as staples, tapes and adhesives.³

Quixil (Omrix Biopharmaceuticals, Ramat Gan, Israel) is a human fibrin sealant consisting of two biological components that form a clot within 30 s of placement on the tissue surface. The clot promotes collagen crosslinking and, consequently, wound healing, and is absorbed after a few days. The aim of this study was to determine whether our good preliminary results with Quixil in an animal model could be extrapolated to human eyes.

Brief report

The study group consisted of five (three male, two female) adults aged 64–70 years (mean 68 (standard deviation (SD) 6.5) years) with endstage, drug-refractory glaucoma (five eyes): neovascular in two (due to central retinal vein occlusion or proliferative diabetic retinopathy), primary open angle in one and pseudoexfoliative in two. All had raised IOP, visual acuity worse than hand movement, painful eye owing to raised intractable IOP and a total optic disc cup. A peripheral iridectomy had not been carried out in these cases owing to the open-angle nature of glaucoma or extensive rubeosis iridis. Informed consent was obtained before the procedure. The study was approved by the institutional ethics committee.

Eyes were anaesthetised with topical oxibuprocaine hydrochloric acid 0.4%. A fornix-based conjunctival flap was created in the superotemporal or superonasal quadrant, and a scleral flap was formed up to the clear cornea. Two-minutes application of mitomycin C 0.04% solution to the exposed scleral surface and external eye irrigation were followed by paracentesis to the anterior chamber. Deep sclerectomy and peripheral iridectomy were carried out. The scleral flap was attached with Quixil Omrix Biopharmaceuticals, and the conjunctival flap was pulled and glued above it.

Postoperatively, patients were treated with topical corticosteroids and chloramphenicol eye drops. No drug was prescribed for glaucoma.

All eyes were biomicroscopically examined preoperatively, on postoperative days 1–3, and then weekly for 1 month, monthly for 2 and 3 months, and thereafter every 3 months to 1 year. The mean duration of follow-up was 1 year. The main outcome measures were a change in IOP, presence of an active filtering bleb, wound leakage (Seidel test),

and intraoperative and postoperative complications.

Preoperative visual acuity ranged from hand movements to no light perception; mean preoperative IOP was 40 (SD 8) mm Hg.

No intraoperative complications were found. One patient with primary open-angle glaucoma had a shallow anterior chamber and choroidal effusion with a negative Seidel test on the first postoperative day, which resolved within 3 weeks after topical treatment with atropine sulphate and dexamethasone drops.

All five patients showed a diffuse active filtering bleb following surgery, with no signs of leakage (fig 1). No patient needed digital massage on the postoperative days. IOP decreased considerably in all patients in the first postoperative month (mean 14 (SD 3.5) mm Hg). In two patients, it increased to 30 mm Hg in the second month and then normalised in one of them with topical antiglaucoma treatment for glaucoma. The other three patients remained treatment free, with an IOP of 10–20 mm Hg at 1 year. Visual acuity was stable in four patients, but deteriorated from light perception to no perception in the patient with pseudoexfoliative glaucoma.

Comments

Fibrin adhesive is theoretically amenable to trabeculectomy, as it mimics physiological sealing processes. It has been used so far in trabeculectomy to manage leaks and hypotony or for closure of conjunctival wounds, with good results.^{4–8} To our knowledge, this is the first use of fibrin adhesive instead of sutures for scleral as well as conjunctival wound closure in penetrating trabeculectomy. Grewing and Mester⁹ described a temporary tamponade of the scleral flap with subconjunctival fibrin glue in two patients with post-trabeculectomy hypotony, in whom the sclera and conjunctiva were primarily sutured.

We found the fibrin adhesive to be safe and effective, forming a smooth seal around the edge of the wound. Additionally, pushing the conjunctiva away from the sclera temporarily prevented scleroconjunctival fibrosis and allowed for bleb formation. Its use simplified the procedure and decreased operating time.

Figure 1 Anterior segment photograph 7 days after trabeculectomy surgery with fibrin adhesive, showing a diffuse active filtering bleb, with local conjunctival hyperaemia.

No postoperative complications were found, and overall outcome was good.

Further investigations with a prospective controlled, randomised study and longer follow-up are still needed.

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Exclusion of COL8A1, the gene encoding the α_2 (VIII) chain of type VIII collagen, as a candidate for Fuchs endothelial dystrophy and posterior polymorphous corneal dystrophy

Fuchs endothelial corneal dystrophy (FECD) MIM#136800 and posterior polymorphous corneal dystrophy (PPCD) MIM#122000 both belong to the corneal endothelial dystrophies in which endothelial dysfunction can lead to corneal oedema. In addition, they both share the common features of endothelial metaplasia and the secretion of an abnormal Descemet's membrane as a pathological posterior collagenous layer (PCL) with a small or absent posterior non-banded zone.^{1,2}

The exact cause of both FECD and PPCD is still unknown, although both are thought to be the result of a disorder of neural crest

Figure 1 Sequence variations in two patients with Fuchs endothelial corneal dystrophy.

terminal differentiation.³ Mutations in *COL8A2*, the gene for the α_2 (VIII) chain of type VIII collagen, have previously been described in patients with both FECD and PPCD,^{4,5} and type VIII collagen is found in both normal anterior banded Descemet's membrane and in the PCL of patients with both FECD and PPCD.⁶ In vivo type VIII collagen may exist as homotrimers or heterotrimers of both α_2 (VIII) and α_1 (VIII) chains.^{7,8} Therefore *COL8A1*, the gene for the α_1 (VIII) chain of type VIII collagen, was an ideal candidate for both FECD and PPCD.

DNA was made available for analysis from 141 unrelated patients with either FECD ($n = 124$) or PPCD ($n = 17$). Data for age of onset were available from 102 (72%) patients with FECD and gave a mean age of onset of 63 (standard deviation (SD) 11) years. Mutation screening of the coding region and part of the surrounding non-coding region of *COL8A1* was carried out for all patients and identified two sequence variations in two different patients with FECD (fig 1; table 1). Both are presumed to be non-pathogenic as neither are likely to alter splicing nor alter the amino acid sequence for the α_1 (VIII) chain of type VIII collagen.

These results suggest that *COL8A1* is unlikely to be implicated in the aetiology of

either FECD or PPCD, although the possibility of pathogenic changes within the promoter region of *COL8A1* cannot be excluded at this time.

In a study of 116 patients with FECD, possible pathogenic mutations were found in 9 (8%) patients and in only one family with PPCD.⁴ This suggests the presence of genetic heterogeneity, and therefore possible pathogenic mutations may not have been found in the present study as not enough patients were examined. This, however, seems unlikely as both studies used a similar number of patients.

These results also support the hypothesis that type VIII collagen exists in vivo as homotrimers of either α_1 (VIII) or α_2 (VIII) and not as heterotrimers. In vitro translation studies supplemented with semi-permeabilised cells have shown that it is possible for type VIII collagen to consist of heterotrimers.⁸ Conversely, immunolocalisation studies by Greenhill *et al.*⁷ using chain-specific antibodies showed different localisation patterns for the two type VIII collagen chains in the human cornea. This, coupled with the results of the present study, suggests that type VIII collagen exists as homotrimers within the cornea and that each performs a different function.

In conclusion, we have excluded the *COL8A1* gene as a candidate for both FECD and PPCD. Analysis of FECD families not showing linkage to the *COL8A2* locus will enable the identification of other candidate genes.⁴ In addition, genes associated with the pathogenesis of PPCD remain to be identified within the *PPCD1* and *PPCD3* loci on chromosome 20 and chromosome 10, respectively.^{9,10}

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Table 1 Sequence variations in *COL8A1*

Diagnosis	Sequence change	Amino acid change	Description
FECD	1860C>T	A620A	Silent polymorphism
FECD	2240delT	–	After the end of coding sequence

Changes numbered according to Genbank accession number NM_001850. FECD, Fuchs endothelial corneal dystrophy.