BIOENGINEERING

Recombinant collagen implants continuing to show promise

by Roibeard O’hEineachain in Vienna

A bioengineered human cornea substitute may have an important role to play in alleviating world blindness in the not too distant future, according to Per Fagerholm MD, University Hospital, Linköping, Sweden.

Speaking at the XXIX Congress of the ESCRS, Dr Fagerholm said that the results of a phase 1 clinical study with the biosynthetic cornea remain very encouraging at three years of follow-up, and further refinements in the production of the corneal substitute material may improve results.

“The reason why we do this is that there is a lack of donor corneas world-wide which is immense. There are 10 million people blind from corneal disease. With this cell-free construct you eliminate the risk of infection from donor to recipient and you also eliminate the risk of immune rejection, which accounts for the majority of the 10 per cent of grafts that are lost within two years of transplantation, according to the Swedish National Cornea Register,” Dr Fagerholm said.

The study involved 10 patients, nine with keratoconus and one with a deep corneal scar. All had undergone anterior lamellar keratoplasty involving implantation of the biosynthetic cornea. The biosynthetic material is composed of human recombinant type III collagen cross-linked with water-soluble carbodimides.

Dr Fagerholm noted that at 24 months’ follow-up, the biosynthetic implants remained stably integrated and avascular, and there were no cases of immune rejection. In addition, the epithelial surface barrier was established by two months and remained stable throughout follow-up.

Moreover, corneal sensitivity was as good as or better than occurs with conventional grafts and tear production was sufficient. Furthermore, in-vivo confocal microscopy showed that the growth of nerves into the implant was more rapid and more complete than is the case with conventional corneal grafts. “We saw that the neural fibres reached the centre of the graft, which is something that does not occur in penetrating keratoplasty,” Dr Fagerholm said.

On the other hand although there was a good colonisation of the implant with host keratocytes, it was a little slower than that commonly seen with donor grafts.

Dr Fagerholm noted that at 24 months spectacle-corrected visual acuity was not as good as that achieved in eyes with conventional corneal grafts, and at two years’ follow-up had a mean value of only 20/110.

When performing the implantation procedure, Dr Fagerholm and his associates first excised a central deep lamellar button 6.0mm in diameter from the patients’ eyes and replaced it with a custom-shaped biosynthetic lamellar button 6.25mm in diameter and 500 µm in thickness.

They secured the button with six overlying sutures and a bandage lens. Postoperatively, patients received topical therapy with chloramphenicol and dexamethasone for eight to 10 weeks. Sutures were removed at six weeks. In a couple of patients there were problems with re-epithelialisation, which appeared to be suture related. One case of poor re-epithelialisation resulted in corneal melting, he noted.

A decade of research

The biosynthetic cornea is a collaborative effort between Dr Fagerholm’s team in Sweden and the Eye institute in Ottawa Canada under the direction of Prof May Griffith PhD. It has so far involved eight years of research, with extensive safety testing and refinement of the biosynthetic material.

The theory behind the recombinant human collagen grafts is based on the observation that when the cornea becomes depleted of keratocytes as a result of intense ultraviolet exposure, as in the case of eyes with UV keratitis, the extracellular matrix is unaffected and the central cornea quickly becomes populated without any loss of corneal transparency.

By mimicking the molecular structure of corneal collagen, the bioengineered grafts serve as scaffolding for the colonisation of the central cornea by keratocytes. The decision to use type III human collagen, which is found in the skin, rather than type I collagen that is found in the cornea, was based on its superior mechanical properties and its lower cost.

The phase 2 study will address some of the complications seen in the phase 1 study.

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