Japanese researchers propose “revolutionary change” to prevent corneal haze after laser surgery

Cell sheet transplants after PRK and LASIK may reduce corneal haze

New research from Japan has shown that transplanting sheets of tissue-engineered epithelial cells to the cornea may prevent patients from developing corneal haze after excimer laser keratectomy.

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The research findings were announced by Dr Yasutaka Hayashida and Dr Yasuo Tano of the Department of Ophthalmology at the Osaka University Medical School in Japan. The findings appeared in the February 2006 edition of Investigative Ophthalmology & Visual Science (2006:47:552-557).

Although excimer laser keratectomy has been established as effective, refractive surgeons know all too well such postoperative complications as eye pain, late recovery of vision, prolonged use of steroids, and corneal haze. Studies indicate that corneal haze occurs more frequently in eyes that require a large amount of correction. For the most part, such patients are often not aware of an opacity until it becomes quite obstructive and begins to impact on their visual acuity. In many cases, corneal haze decreases and disappears within six to nine months. However, in a certain proportion of patients, the haze can persist and cause the vision to deteriorate.

In cases of high myopia that require a larger refractive change, recurrent corneal haze can become resistant to medical treatment and may require further laser photoblation.

Corneal haze is essentially caused by the cornea’s wound response. The haze or opacity is thought to arise from the biochemistry that occurs at the junction between the epithelium and the stroma. Against such a background, the Japanese researchers aimed to enhance wound healing at this site by transplanting tissue-engineered corneal epithelial cell sheets directly after excimer laser ablation.

The tissue-engineered cell sheets consist of stratified epithelial layers that closely resemble the native corneal epithelium. Due to the fact that the cells are cultured and harvested as intact cell sheets together with their deposited extracellular matrix (ECM), they attach themselves directly to the corneal stroma without the need for sutures.

Animal Study

To conduct their experiments, the Japanese research group removed a 5 mm x 5 mm corneal biopsy from 40 New Zealand rabbits. The cells were incubated at 37ºC; suspended cells were cultured under temperature responsive culture conditions from which a monolayer was formed after one to two weeks. At that point, the researchers harvested a cell sheet from each biopsy.

To test the effectiveness of the cell sheets on post-surgical outcome, the researchers used a 193 nm argon fluoride excimer laser to create a 7 mm diameter ablation zone with a depth of 160 µm in 40 rabbits. Of the 40 animals, 19 animals received a transplantation sheet immediately following the excimer laser photoblation; 21 of the animals served as controls.

Following experimental cell sheet transplantation, the entire ocular surface was covered with a custom-made hard contact lens to provide postoperative healing protection. Transplant sheets of cultured cells were stained with a fluorescent cell tracer dye, known as “Dil I,” to assist observation.

Slit-lamp microscopic exams were performed daily until corneal re-epithelialisation was completed and then weekly for up to two months after the operation. Quantification of corneal haze was scored in a masked fashion by three grading scale.

Immediate re-epithelisation

According to the researchers “eyes receiving conventional laser ablation required 3 to 5 days to become completely re-epithelialised.” By contrast, corneal surfaces of cell-sheet transplanted eyes demonstrated a complete and intact epithelial layer immediately after cell sheet attachment, with no defects present,” the researchers reported.

Eyes that had received cell sheet transplants were scored as having generally mild haze at 1 and 2 months after surgery; however, the eyes of the rabbits in the control group showed more severe degrees of corneal haze throughout the follow-up period.

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A statistical analysis of postoperative corneal haze showed a significant inhibition of haze in the cell sheet transplanted eyes compared to the control eyes. In addition, signs of apoptosis were observed in the control group, but not the transplant group.

The research report may indicate a significant advantage for the cell transplantation approach because the ablated corneal surfaces are completely re-epithelialised immediately after keratectomy, whereas control eyes generally required three to five days to become re-epithelialised. This delay of three to five days likely contributes to the postoperative pain and corneal haze associated with excimer laser photoblation, which, of course, significantly affects the patient’s quality of life.

Consequently the authors state that the “use of cell sheet keratoplasty and its ability to inhibit postoperative corneal haze may therefore initiate a revolutionary change in our methods for the correction of refractive errors and the treatment of superficial corneal opacities.”

Further data outlined by the researchers showed that when the observed hyperplasia had begun to decrease after two months, there was an accumulation of aSMA and collagen III demonstrating the presence of myoblasts and activated keratocytes. In addition, enhanced ECM deposition activities may further contribute to the development of corneal haze.

Overall, “use of cell sheet keratoplasty after laser ablation seemingly provides several distinct advantages over the traditional methods of PRK, PTK [phototherapeutic keratectomy] and LASIK, by allowing for rapid visual recovery and a reduction in both postoperative eye pain and corneal haze,” the researchers concluded.

“Cell sheet keratoplasty offers an important breakthrough in the field of refractive surgery” to inhibit postoperative corneal haze, the researchers concluded.

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Glossary

- 3T3 feeder layers: feeder cells are used to support the growth of a variety of cell types; such cells are normal but have been inactivated by gamma-irradiation. The cells serve as a basal layer for other cells and supply important metabolites without further growth or division of their own.

- Mitomycin C: any of a group of antimitobalines produced by Streptomyces caespitosus that is capable of inhibiting DNA synthesis.

- aSMA: alpha smooth muscle actin produced by myoembryonic cells capable of fusion with other cells.

- Keratocytes: fibroblastic stromal cell of the cornea.

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