Minimizing corneal endothelial damage due to intraocular lens contact. SCOTT KIRK, RONALD M. BURDE, AND STEPHEN R. WALTMAN.

Previous studies have shown that momentary contact between a methylmethacrylate intraocular lens and the corneal endothelial cells results in extensive cell damage. This contact damage is reduced by coating the pseudophake with various solutions prior to contact with the endothelium. Following clinical intraocular lens implantation there is rapid corneal endothelial cell loss.1 Such loss, which may be severe, is permanent because of limited endothelial cell regeneration. Normally, cell enlargement and spreading compensate for cell loss.2 This depletion of the endothelial reserve probably accounts for the early and late corneal edema that may follow intraocular lens implantation. Since brief contact between the polymethylmethacrylate intraocular lens and the corneal endothelium results in 20 to 35 percent cell loss,3 protective solutions may be useful for coating these lenses and reducing cell damage. This study examines the efficacy of various solutions in preventing endothelial damage following pseudophake-endothelial contact.

Methods and materials. Adult albino rabbits were sacrificed by an overdose of intravenous pentobarbital. Following enucleation the corneas were removed, with a 1 mm. rim of attached sclera. They were placed on a specially fitted concave Teflon block, endothelial side up. Aqueous humor was removed by tilting with a Weck-Cel sponge placed at the margin. A Medallion intraocular lens (Medical Workshop, Holland), previously immersed in one of the test solutions for 1 min., was then gently placed on the endothelium for 1.5 min. Endothelium cell damage was determined by trypan blue (TB) staining and scanning electron microscopy (SEM).

A solution of 0.25 percent TB in normal saline was used to cover the endothelium. After 90 sec. the dye was removed, and the corneas passed through two changes of saline. Dye enters and stains only those cells whose membrane permeability has been disrupted. Endothelial cell damage was measured by the percentage of stained cells viewed under low power. All readings were done by two observers who were unaware of the previous treatment of the cornea.

Table I. Endothelial cell loss after pseudophake contact

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean cell loss (%)</th>
<th>S.E.M.*</th>
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</thead>
<tbody>
<tr>
<td>None</td>
<td>43.33</td>
<td>4.23</td>
</tr>
<tr>
<td>Normal saline</td>
<td>24.17</td>
<td>2.37</td>
</tr>
<tr>
<td>Plasma</td>
<td>21.66</td>
<td>2.64</td>
</tr>
<tr>
<td>TC199</td>
<td>20.83</td>
<td>3.19</td>
</tr>
<tr>
<td>Albumin</td>
<td>14.58</td>
<td>1.89</td>
</tr>
<tr>
<td>Serum</td>
<td>10.00</td>
<td>1.07</td>
</tr>
</tbody>
</table>

N = 12 for each group.

Corneas were fixed in 2.7 percent glutaraldehyde buffered in 0.2M sodium cacodylate. They were dehydrated in increasing concentrations of ethyl alcohol and finished in the critical point apparatus. The specimens were coated with palladium-gold and viewed with the Cambridge Stereoscan Mark 2A scanning electron microscope. The solutions evaluated were normal saline, salt-poor human albumin, TC-199 medium with 5 percent dextran, and human serum and plasma drawn daily. Corneas on which the lens was applied dry were used as controls.

Results. Test solutions placed on the rabbit corneal endothelium for 1.5 min. did not result in damage apparent by TB staining or SEM.

A dry Medallion lens placed on each of 12 corneas for 1.5 min. caused extensive cell damage (mean, 45 percent) as estimated by TB staining. SEM confirmed the endothelial cell damage due to disruption of the surface membranes. Areas corresponding to the edge of the lens showed complete endothelial loss (Fig. 1, A and B).

Twelve corneas were used to evaluate each of the five substances. The pseudophake was placed in solution for 1 min. and then placed onto the corneal endothelium for 1.5 min. The corneas were immediately stained and fixed. The results are shown in Table I. Significant differences exist between the dry lens and lenses coated with any of the substances tested (p <0.001). No appreciable difference could be found between the protective effects of normal saline, plasma, or TC-199. The mean cell damage was approximately 20 to 25 percent in all cases. The use of albumin (mean damage, 15 percent) caused less damage than that of normal saline (t = 3.16; p <0.005) or plasma (t = 2.18; p <0.05). Lenses first placed in sera caused the least amount of cell destruction (mean damage, 10 percent), with a
Fig. 1. Scanning electron micrograph of rabbit corneal endothelium following contact with a dry intraocular lens. A, Cell surface membranes have been damaged. (×1,000.) B, Area of contact of corneal endothelium and edge of dry intraocular lens. Complete loss of cell membranes is evident. (×500.)
Fig. 2. Scanning electron micrograph of endothelium following contact with implant placed in plasma. (x1,000.)

Fig. 3. Scanning electron micrograph of endothelium following contact with lens placed in normal saline. (x1,000.)
significant difference between its use with that of normal saline, plasma, or TC-199 (p <0.005 in all cases) or albumin (t = 2.11; p < 0.05).

Two samples from each of the five tested substances were studied by SEM. Areas of membrane destruction were found in all the corneas. The type and pattern of damage was the same with all substances tested, the difference being the number of affected areas. This correlated well with the results of TB-stained corneas (Figs. 2 and 3).

Discussion. This study confirms the findings of Kaufman and Katz that extensive damage results from contact between a methylmethacrylate intraocular lens and the corneal endothelium. Placing the intraocular lens in salt-poor human albumin or serum prior to endothelial contact resulted in a significant reduction in endothelial damage when compared to placing it in normal saline. The increased viscosity and protein composition of these solutions may account for the difference. Serum is more efficacious than plasma, suggesting that the fibrinogen or heparin in plasma negates some of the protective effect.

During surgery, contact between the intraocular lens and the corneal endothelium is often unavoidable, especially in cases of shallow anterior chambers. This study suggests that the use of human albumin or the patient’s own serum to coat the intraocular lens prior to insertion may protect the corneal endothelium. Since both of these substances are easily obtainable in a sterile fashion, a clinical trial may be indicated. Prevention of damage to the corneal endothelium during surgery may reduce corneal edema and eliminate some of the problems of intraocular lens placement.

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Key words: intraocular implants, corneal endothelium.

REFERENCES

Enzyme-synthetic approach to demonstration of phosphorylase activity in the living rabbit cornea. Tsugio Amemiya and Hidehiko Yoshida.

An enzyme-synthetic method of demonstrating phosphorylase was applied to the living rabbit cornea, and polyglucose particles synthesized from glucose-1-phosphate in vivo were studied electron microscopically. In the corneas in which the medium for phosphorylase was applied from the anterior chamber or the bulbar subconjunctiva, synthesized polyglucose particles were found in the cytoplasmic matrices of the epithelium. When the medium was deposited in the conjunctival sac, a few synthesized polyglucose particles were found in the cytoplasmic matrices of only the superficial layer of the corneal epithelium. These findings suggest that metabolites for glycogen metabolism come mainly from the aqueous humor in the anterior chamber. The polyglucose particles synthesized by the enzyme-synthetic method in vivo resemble native glycogen particles. In addition, these particles were not overproduced because the synthesis of polyglucose is probably regulated in vivo.

There are three pathways by which metabolites reach the cornea from the surrounding media: (1) across the corneal limbus with the blood capillaries in the peripheral conjunctiva and sclera; (2) across the endothelium with the aqueous humor in the anterior chamber; (3) across the epithelium with the tear film. Phosphorylase is related to the following reaction:

\[ \text{glucose-1-phosphate} + (\text{glucose})_n \rightarrow (\text{glucose})_{n+1} + \text{inorganic phosphate} \]

It has been believed for some time that phosphorylase is a glycolytic and glycogenetic enzyme in vivo. However, at the present time, this enzyme is assumed to play a glycolytic role in vivo in glycogen metabolism. The enzyme-synthetic method applied to the living chick retina could demonstrate that polyglucose particles were synthesized in vivo from glucose-1-phosphate by the action of phosphorylase and branching glycosyltransferase. The findings obtained with this method are considered to be very similar to the condition in the living cell. When a large amount of glucose-1-phosphate is placed in any of the above-mentioned three pathways of metabolites in the cornea, polyglucose may be expected to be synthesized from glucose-1-phosphate by the action of phosphorylase and branching enzyme if these enzymes exist in the corneal epithelium and stromal keratocytes. The experiments described here were therefore undertaken to apply the media for histochemical demonstration to these three routes separately. The present paper clarifies the metabolic path-