Prospective, Randomized Clinical Evaluation of Optisol vs Organ Culture Corneal Storage Media

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Objective: To compare the outcome of penetrating keratoplasty with the use of corneas stored either in Optisol (Chiron Ophthalmics, Irvine, Calif) or in organ culture.

Methods: Penetrating keratoplasty was performed on 12 pairs of patients matched by age and diagnosis. Each pair of procedures was done on the same day by the same surgeon using the same technique. Twelve pairs of corneas were used. One cornea of each pair had been stored in organ culture at 36°C and one in Optisol at 4°C. Mean (±SD) storage time was 6±3 days. Mean endothelial cell density before storage was 2617/mm² for the corneas in organ culture and 2624/mm² for the corneas in Optisol. Examinations were performed at 1, 4, 12, and 24 months.

Results: One reversible rejection occurred in the Optisol group. At 1 month the mean endothelial cell density was 2327±341/mm² for the organ culture group and 2240±504/mm² for the Optisol group. At 12 months the difference was more pronounced (2225±410 and 2103±466/mm², respectively), although statistically not significant. Corneal thickness also did not show any statistically significant difference.

Conclusion: Penetrating keratoplasty performed with corneas stored for a maximum of 11 days in either Optisol or organ culture show similar outcomes in the first 2 postoperative years.


An ideal corneal storage medium should preserve endothelial viability during prolonged storage and be reasonably priced. Optisol (Chiron Ophthalmics, Irvine, Calif), a corneal storage medium used at 4°C and containing 2.5% chondroitin sulfate, 1% dextran, vitamins, and precursors of adenine triphosphate, is widely used, especially in the United States. Corneas can be stored in this medium for up to 2 weeks. More recently, Optisol GS at 4°C has been reported to preserve endothelial function up to 21 days. In Europe, long-term preservation in organ culture at 36°C is preferred. The advantages of organ culture preservation include longer storage times and an improved ability to diagnose infections before transplantation. The major advantage of organ culture is the extension of postmortem time, which increases the donor pool. The disadvantages are the need for trained personnel, the risk of possible alterations in the components of the fetal calf serum used, and concerns regarding the use of fetal calf serum in countries with bovine spongiform encephalitis. The average costs per cornea, although comparable, are somewhat lower for organ culture corneas.

The purpose of this study was to compare prospectively and in the long term the clinical results of penetrating keratoplasties (PKPs) with paired corneas stored in either organ culture or in Optisol with the same duration of preservation.

Results

Donor and Recipient Characteristics

Between August 1, 1994, and January 31, 1997, 12 pairs of corneas were used, supplying material for PKPs in 24 patients. Mean storage time was 6±3 days, with a maximal storage of 11 days. There were no statistically significant differences in the mean endothelial cell densities before storage (Table 1; P = .89). During storage, the mean endothelial cell loss in the organ culture–stored corneas was 5%. (The endothelial cell count for the Optisol group was performed only at the beginning of storage.) The mean graft trephine size was 7.9±1.3 mm and the
PATIENTS AND METHODS

Twelve paired donor eyes, enucleated between 2 and 47 hours post mortem (mean, 24 hours) were used for the study. Mean donor age (±SD) was 49.9±13.9 years (range, 33-74 years). After the corneoscleral buttons were harvested and the epithelium, keratocytes, and endothelium were evaluated with a phase-contrast microscope, 1 cornea of each pair was stored in organ culture medium at 36°C and the fellow cornea in Optisol at 4°C. Endothelial cell count was performed with a fixed-frame counting technique after a photograph was taken. The magnification of the phase-contrast microscope was calculated with a Neubauer hemocytometer.

The organ culture contained minimum essential medium and fetal calf serum and was supplemented with penicillin, streptomycin, and amphotericin B.4

Before transplantation, the cornea stored in organ culture was deswelled with 6% dextran T300 overnight and the endothelium was examined with phase-contrast microscopy on the morning of surgery. The Optisol-stored corneas were examined only before preservation. The paired corneas were then transplanted in a prospective, randomized fashion (random list in eye bank). Each pair of recipients had been matched for diagnosis and age. High-risk cases and unwillingness to participate in a long-term follow-up were exclusion criteria. Subjects were enrolled after signing an informed consent.

Table 1 summarizes the characteristics of the patients in both groups. The PKPs on each matched pair of recipients were performed by the same surgeon (B.E.F. or M.B.) on the same day (within 2 hours), using the same graft size and the same technique, which included the use of a mechanical trephine, viscoelastics, and 10-0 nylon sutures. Because the Optisol-stored corneas are more opaque than the organ culture–stored corneas, masking of the donor surgeon as to preservation method was not possible.

Topical corticosteroids were given postoperatively 4 to 5 times daily and tapered until suture removal 1 year after keratoplasty. Prospective clinical evaluation, including pachymetry with an ultrasonic pachymeter (DGH-1000; DGH Inc, Exton, Pa) and endothelial cell count with a noncontact specular microscope (SP 1000; Topcon, Tokyo, Japan), was performed at 1, 4, 12, and 24 months. Fixed-frame counting technique was used to calculate endothelial cell density according to instructions and the magnification provided by the manufacturer. Endothelial cell loss was calculated by expressing the difference between prepreservation and postoperative densities as a percentage of the prepreservation count (assuming that the magnification of the camera provided by the manufacturer is correct). Best-corrected visual acuity (BCVA) was determined with spectacles and without contact lenses. Visual acuity tests were not standardized. Graft clarity was assessed at the slitlamp and was rated on a scale from 1 to 4, with 1 being clear and 4 totally opaque. Investigators were masked.

When a patient dropped out of the study, the follow-up for the paired recipient was also discontinued at the same time. The sample size of 10 corneas in each group would have been great enough to detect a statistical significance (P<.05, .2 level) assuming an expected size difference of 450 cells per square millimeter and an SD of 350 cells per square millimeter. The paired 2-tailed t test was used to compare the two groups. Unless otherwise specified, all data are given as mean±SD.

Table 1. Demographics of Recipients and Donor Endothelial Cell Density

<table>
<thead>
<tr>
<th></th>
<th>Organ Culture Group</th>
<th>Optisol Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean ± SD</td>
<td>44.1 ± 18.2</td>
<td>45.8 ± 17.1</td>
</tr>
<tr>
<td>Sex, No. F/M</td>
<td>4:8</td>
<td>4:8</td>
</tr>
<tr>
<td>Donor endothelial cells</td>
<td>2617 ± 395</td>
<td>2624 ± 333</td>
</tr>
<tr>
<td>before storage, cells/mm², mean ± SD</td>
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</table>

In the first 3 days after keratoplasty, epithelial defects were present in 4 corneas (33%) in the organ culture group and in 7 (58%) in the Optisol. Every erosion healed before the fourth day. There were no late-onset erosions. Graft clarity assessed by slitlamp examination in the first days after surgery showed a less transparent cornea in the Optisol group.

There were no cases of graft failure. One case of reversible graft rejection at 24 months occurred in a patient with keratoconus in the Optisol group. Because of severe astigmatism after suture removal, arcuate keratotomies (2 in each group) and wedge resection (1 in the Optisol group) had to be performed. Secondary glaucoma occurred in 1 eye in each group and cataracts developed at 24 months in 1 eye (organ culture group). Because of wound dehiscence after suture removal, the graft was resutured in a 29-year-old patient in the Optisol group who had undergone grafting because of herpetic keratitis.

Visual acuities were similar in both groups in the later stage of follow-up. Because of amblyopia, the visual acuity results of 1 matched pair were omitted. At 1 month, only 9% of the Optisol group but 45% of the or-

mean recipient bed trephine size was 7.6±1.5 mm for both groups.

Preoperative diagnoses were the same in each matched patient pair and included keratoconus (8 pairs), Fuchs endothelial dystrophy (2 pairs), pseudophakic bullous keratopathy (1 pair), and herpetic keratitis (1 pair). Mean age at time of surgery was not significantly different in the 2 groups, being 44.1±18.2 years for the organ culture group and 45.8±17.1 years for the Optisol group (P=0.40). In a single pair, PKP, extracapsular cataract extraction, and lens implantation were performed. In both groups, 50% of the eyes had BCVA of 20/100 or worse before keratoplasty.

Mean follow-up was 25.2±12.9 months. One patient in each group died between 3 and 4 months postoperatively. The fellow recipients were excluded from further study.

CLINICAL OUTCOME

In the first 3 days after keratoplasty, epithelial defects were present in 4 corneas (33%) in the organ culture group and in 7 (58%) in the Optisol. Every erosion healed before the fourth day. There were no late-onset erosions. Graft clarity assessed by slitlamp examination in the first days after surgery showed a less transparent cornea in the Optisol group.

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Visual acuities were similar in both groups in the later stage of follow-up. Because of amblyopia, the visual acuity results of 1 matched pair were omitted. At 1 month, only 9% of the Optisol group but 45% of the or-
gan culture group had BCVA of 20/40 or better (Table 2). At 12 months postoperatively, 78% of the eyes in both groups had reached a BCVA of 20/40 or better.

PACHYMETRY AND ENDOTHELIAL CELL DENSITIES

Pachymetry values remained relatively constant (range of mean corneal thickness, 530-576 µm) in the organ culture group during the follow-up period. In the Optisol group, because of 1 late reversible rejection episode with marked stromal edema, and because of the small number of corneas measured at 24 months (8 pairs), mean corneal thickness was considerably but not significantly higher at 24 months (582±78 µm).

The endothelial cell density decreased with time in both groups, with a steeper decline for the Optisol group between 12 and 24 months. Pachymetry and endothelial cell densities at different postoperative times failed to reach statistical significance between the 2 groups (Table 3 and Table 4).

COMMENT

This prospective, randomized, long-term clinical study showed that, up to 24 months after penetrating keratoplasty, there were no differences in outcome between corneas that were stored in organ culture or in Optisol for a maximum of 11 days.

The recipients of corneas in the organ culture group had a faster visual rehabilitation, with 45% of the eyes attaining BCVA of 20/40 or better at 1 month postoperatively, compared with 9% in the Optisol group. One late-onset reversible rejection occurred in the Optisol group, but it failed to cause a significant difference between the 2 groups.

Previous studies have prospectively compared different corneal storage media and systems. Compared with corneas stored in DexSol (Chiron Ophthalmics), Optisol-stored corneas have been shown to be thinner after PKP.1,14 Moll et al15 and Rijneveld et al16 could not find any difference between corneas stored in organ culture at 31°C and corneas stored in McCarey-Kaufman (MK) medium. De Beijer-Dominicus et al17 reported that eyes transplanted with organ culture–stored corneas had lower visual acuities than eyes that had received corneas stored in MK medium.17

A retrospective study comparing endothelial cell loss in corneas stored either in MK medium or in organ culture reported that, 2 months after PKP, organ culture–stored corneas showed a 28% loss and MK-stored corneas, a 10% loss.18,19 However, in that study, all corneas were initially placed in MK medium 24 hours before storage in organ culture and thereafter restored in MK medium before transplantation. The greater cell loss in the organ culture group may have been caused by metabolic changes associated with the repeated changes of medium and temperature. The same group of authors, after supplementing the organ culture medium with 1.35% chondroitin sulfate, described a similar endothelial cell loss 2 months after PKP with the use of organ culture or MK medium in a nonrandomized fashion.20

The mean storage time in this study was relatively short (6 days). Therefore, we cannot exclude the possibility that longer storage times could result in a different clinical outcome, which would clearly favor organ culture when preservation periods longer than 2 weeks are used. The limitation of our study was the relatively small sample size (12 pairs of corneas).

On the basis of our findings, we conclude that organ culture and Optisol are equivalent systems for the successful short- to medium-term storage of human cor-

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### Table 2. Postoperative Best-Corrected Visual Acuity

<table>
<thead>
<tr>
<th>Time, mo</th>
<th>No. of Pairs</th>
<th>Organ Culture Group</th>
<th>Optisol Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>5 (45)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>8 (80)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
<td>7 (78)</td>
<td>7 (78)</td>
</tr>
<tr>
<td>24</td>
<td>7</td>
<td>5 (71)</td>
<td>5 (71)</td>
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</tbody>
</table>

### Table 3. Postoperative Pachymetry Results

<table>
<thead>
<tr>
<th>Time, mo</th>
<th>No. of Pairs</th>
<th>Corneal Thickness, µm, Mean ± SD</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>555 ± 49</td>
<td>.40</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>530 ± 53</td>
<td>.13</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
<td>526 ± 49</td>
<td>.18</td>
</tr>
<tr>
<td>24</td>
<td>8</td>
<td>569 ± 57</td>
<td>.69</td>
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</table>

*Paired 2-tailed t test.

### Table 4. Postoperative Endothelial Cell Density

<table>
<thead>
<tr>
<th>Time, mo</th>
<th>No. of Pairs</th>
<th>Organ Culture Group</th>
<th>Optisol Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>2327 ± 341</td>
<td>2240 ± 504</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>2266 ± 296</td>
<td>2190 ± 575</td>
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<tr>
<td>12</td>
<td>10</td>
<td>2225 ± 410</td>
<td>2103 ± 466</td>
</tr>
<tr>
<td>24</td>
<td>7</td>
<td>1938 ± 509</td>
<td>1743 ± 474</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Time, mo</th>
<th>No. of Pairs</th>
<th>% Cell Loss, Mean ± SD</th>
<th>P*</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>9 ± 11</td>
<td>.60</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>13 ± 9</td>
<td>.70</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
<td>13 ± 13</td>
<td>.40</td>
</tr>
<tr>
<td>24</td>
<td>7</td>
<td>24 ± 21</td>
<td>.40</td>
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*Paired 2-tailed t test.
neas before keratoplasty. Selection of one system over the other should be based on such considerations as facilities, personnel, number of corneas stored, and the need for extended storage times.

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REFERENCES


A look at the past . . .

Elshnig (1931), on reviewing his results with the various intracapsular methods, came to the following conclusions: He abandoned the Smith operation because an iridectomy was always necessary and the loss of vitreous was too great. The Barraquer method was too difficult and caused too much loss of vitreous. He was pleased with the forceps operation and recommended it for general adoption. This maneuver succeeded in 80 per cent of the cases; in 10 per cent the capsule ruptured, and in 10 per cent the forceps did not take hold. Of 468 cases from his clinic, loss of vitreous occurred in 25. The capsule ruptured in 23 cases. In 40 cases the pupil was drawn upward; glaucoma was observed in 5 cases, and detachment occurred in 2 cases.