Epithelial Healing Time and Rate of the Cornea
After Myopic Epikeratoplasty

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This study was performed to investigate the corneal epithelial healing time and
rate according to the method for promoting the reepithelialization after myopic
epikeratoplasty. A prospective study was conducted on 30 myopic epikeratoplasties
which were divided into 3 groups according to the method for promoting the
epithelial healing. The groups consisted of 10 eyes with pressure patches, 10 eyes
with Acuvue® disposable contact lens(CL) and 10 eyes with SeeQuence® disposable
CL.

The corneal epithelial healing time were 3.4, 3.5 and 3.4 postoperative days for the
pressure patch, Acuvue® CL and SeeQuence® CL groups, respectively.

The corneal epithelial healing rates during postoperative 1, 2, and 3 days were
0.33, 0.78, and 0.44 mm2/hour for the pressure patch group; 0.24, 0.92 and 0.37
mm2/hour for the Acuvue® CL group; and 0.30, 0.79 and 0.38 mm2/hour for the
SeeQuence® CL group.

These results suggest that a disposable contact lens may not hinder epithelial
healing compared with a pressure patch.

Key words: corneal epithelial healing, epikeratoplasty, pressure patch, contact lens.

INTRODUCTION

The healing of an acute injury with cell loss in the
corneal epithelium proceeds by means of a
complicated sequence of events. It is well known
that an important part of the repair process is the
sliding of adjacent epithelial cells to cover the
defect.1-6 Thereafter, cell proliferation restores the
normal tissue structure.

Beginning with the work by Friedenwald and

Buschke,2 several investigators have examined the
effects of hormones, therapeutic agents and
pathological conditions on corneal epithelial wound
healing.7-13

However, these studies have yielded a number of
conflicting results, including wide variations in
reported values for the normal rate of wound closure
and the efficacy of a number of drugs to modulate
this process. These inconsistencies may have
resulted from several different factors, including
differences in data analysis, wound size, and the
method used to create the wound.

Epikeratoplasty (epikeratophakia), which was
originally described by Kaufmann,14 is a good
human model to investigate the healing time and
rate of corneal epithelium, because the procedure is
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performed on a 7 mm-diameter deepithelized human cornea.

The purpose of this study was to investigate corneal epithelial healing time and rate after myopic epikeratoplasty according to the methods for promoting reepithelization, such as pressure patches and disposable bandage contact lenses (CL). A prospective study of corneal epithelial healing time and rate was conducted by comparing the period for complete healing and the healing rate of the disposable bandage contact lenses after myopic epikeratoplasty with these of pressure patch.

PATIENTS AND METHODS

A total 30 cases (30 eyes) having epikeratoplasty for myopia were enrolled in this study, and were randomly divided into 3 groups. Each group composed of 10 cases (10 eyes) with myopia, were treated with a different kind of post operative management, such as pressure patches (P), Acuvue® (Johnson & Johnson) disposable contact lenses(A), and SeeQuence® (Bausch & Laumb) disposable contact lenses (S) for epithelial healing. Each group was composed of 10 cases (10 eyes) with myopia.

The age, sex distribution, and refractive power of each group did not show any significant difference (Table 1).

Acuvue® disposable contact lenses have a medium water content (58%), higher than that of plano-T®, and a 0.012 cm lens thickness.

SeeQuence® disposable contact lenses have a low water content (38.6%) and a 0.006 cm thickness, thinner than that of plano-T® (Table 2).

All tissues in this study were commercially prepared Kerato Lens™ (Allergan Medical Optics) and 8.5 mm in diameter of power. All procedures were performed by one surgeon (J.H. Lee). The power of the lenticule was individualized for each patient based on the average keratometry reading, and the spherical equivalent in diopters corrected to the corneal plane. The surgical technique was performed by the Kaufman-McDonald-Epikeratophakia (KME) method. The tissue lens was rehydrated for 20 minutes in a balanced salt solution containing 100 μg of gentamicin per milliliter of solution and was placed on a Delrin block under a protective cover with one drop of the hydrating solution on the stromal surface.

After the retrobulbar anesthesia and Nadbath akinesia, the optical center was marked on the cornea using a 26-gauge needle. Fixation sutures with 4-0 silk were placed through the superior and inferior rectus muscles. A blunted cellulose sponge was soaked in unpreserved 4% cocaine. A Hessburg-Barron vacuum trephine was used to create a 7.0 mm-diameter corneal cut with a depth of 0.2-0.3 mm, and the central island of epithelium (7.0 mm-diameter) was removed. The peripheral lamellar dissection was created at the base of the trephine cut, which extended toward the limbus for 1 mm. The edge of the lens was sutured in place.

Table 1. Age and sex distribution by group

<table>
<thead>
<tr>
<th></th>
<th>Acuvue®</th>
<th>SeeQuence®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age (average years)</td>
<td>21-51 (32.5)</td>
<td>21-46 (30.8)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>5:5</td>
<td>3:7</td>
</tr>
<tr>
<td>Kerato-Lens power</td>
<td>-9-28 (-17.8)</td>
<td>-10-23 (-17.0)</td>
</tr>
</tbody>
</table>

Table 2. Characteristics of contact lenses

<table>
<thead>
<tr>
<th></th>
<th>Acuvue®</th>
<th>SeeQuence®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water Content (%)</td>
<td>58%</td>
<td>38.6%</td>
</tr>
<tr>
<td>Thickness (cm)</td>
<td>0.012</td>
<td>0.006</td>
</tr>
<tr>
<td>Diameter (cm)</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Dk (cm² ml O₂ /sec ml mmHg)</td>
<td>18 × 10⁻¹¹</td>
<td>9 × 10⁻¹¹</td>
</tr>
</tbody>
</table>
with 16 interrupted 10-0 nylon sutures.

Subtenon injection of 20 mg of methylprednisolone acetate (Depomedrol®) and 20 mg of gentamicin were given at the end of the procedure.

Until complete epithelial healing, one of three types of postoperative management to promote epithelial healing was applied-pressure patches, Acuvue® disposable contact lenses, or SeeQuence® disposable contact lenses without any topical application.

Everyday after surgery, we performed a slit lamp examination and a corneal photography (Topcon, Japan) with fluorescein until complete epithelial healing was achieved. To grade epithelial healing, a thin transparent plastic grid divided into 1 square/mm² was placed over the projected image of the fluorescence corneal photography. 0.35% Fluoresoft® was used as a dye (Fig. 1).

Numerical data are presented as the mean ± standard deviation. ANOVA and t-test were used for the statistical analysis.

**RESULTS**

The fluorescein stained area is considered as the unhealed area. The unhealed area on post op 0 day was 38.5mm² for all three groups, which was a deepithelized area of 7mm diameter for epikeratoplasty. The unhealed areas on postop 1st day of the P, A and S groups were 30.7 ± 3.3 mm², 32.7 ± 4.7 mm² and 31.2 ± 3.9 mm² respectively. The unhealed areas on postop 2nd day of the P, A and S group was 11.9 ± 4.1 mm², 10.6 ± 4.1 mm² and 12.3 ± 5.93 mm², respectively. The unhealed areas on postop 3 day of P, A and S group were 1.4 ± 2.2 mm², 1.7 ± 2.0 mm² and 3.1 ± 4.8 mm² respectively.

The corneal epithelial healing was completed in the P, A and S groups at postoperative 3.4 ± 0.5 days, 3.5 ± 0.5 days and 3.4 ± 0.5 days respectively. The difference in the corneal epithelial healing times among the three groups was not statistically significant (ANOVA: p = 0.91).

The corneal healing rate in terms of the decrease in the wound area (mm²/hr) during post-operative

**Table 3. Changes in unhealed area (mm²)**

<table>
<thead>
<tr>
<th>Post-op Day</th>
<th>Pressure Patch</th>
<th>Acuvue®</th>
<th>SeeQuence®</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>38.5</td>
<td>38.5</td>
<td>38.5</td>
</tr>
<tr>
<td>1</td>
<td>30.7 ± 3.3</td>
<td>32.7 ± 4.7</td>
<td>31.2 ± 3.9</td>
</tr>
<tr>
<td>2</td>
<td>11.9 ± 4.1</td>
<td>10.6 ± 4.1</td>
<td>12.3 ± 5.9</td>
</tr>
<tr>
<td>3</td>
<td>1.4 ± 2.2</td>
<td>1.7 ± 2.0</td>
<td>3.1 ± 4.8</td>
</tr>
</tbody>
</table>

**Table 4. Healing rate by wound area (mm²/hr)**

<table>
<thead>
<tr>
<th>Post-op Day</th>
<th>Pressure Patch</th>
<th>Acuvue®</th>
<th>SeeQuence®</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>0.33 ± 0.14</td>
<td>0.24 ± 0.20</td>
<td>0.30 ± 0.16</td>
</tr>
<tr>
<td>1-2</td>
<td>0.78 ± 0.15</td>
<td>0.92 ± 0.17</td>
<td>0.79 ± 0.21</td>
</tr>
<tr>
<td>2-3</td>
<td>0.44 ± 0.13</td>
<td>0.37 ± 0.13</td>
<td>0.38 ± 0.20</td>
</tr>
<tr>
<td>3-4</td>
<td>0.059 ± 0.09</td>
<td>0.073 ± 0.081</td>
<td>0.13 ± 0.20</td>
</tr>
</tbody>
</table>
Table 5. Healing rate by wound radius (mm/hr)

<table>
<thead>
<tr>
<th>Post-op Day</th>
<th>Pressure Patch</th>
<th>Acuvue®</th>
<th>SeeQuence®</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>0.18 ± 0.04</td>
<td>0.14 ± 0.08</td>
<td>0.17 ± 0.06</td>
</tr>
<tr>
<td>1-2</td>
<td>0.28 ± 0.03</td>
<td>0.31 ± 0.03</td>
<td>0.28 ± 0.04</td>
</tr>
<tr>
<td>2-3</td>
<td>0.21 ± 0.03</td>
<td>0.19 ± 0.04</td>
<td>0.20 ± 0.05</td>
</tr>
<tr>
<td>3-4</td>
<td>0.05 ± 0.06</td>
<td>0.06 ± 0.07</td>
<td>0.07 ± 0.10</td>
</tr>
</tbody>
</table>

0-1 day in the P, A and S groups were 0.33 ± 0.14 mm²/hr, 0.24 ± 0.2 mm²/hr and 0.30 ± 0.16 mm²/hr, respectively. The corneal healing rate during post operative 1-2 day in P, A and S groups were 0.78 ± 0.15 mm²/hr, 0.92 ± 0.17 mm²/hr and 0.79 ± 0.21 mm²/hr, respectively. The corneal healing rate during post operative 2-3 day in P, A and S groups were 0.44 ± 0.13 mm²/hr, 0.37 ± 0.13 mm²/hr and 0.38 ± 0.20 mm²/hr, respectively. The corneal healing rate during post operative 3-4 day in P, A and S groups were 0.059 ± 0.09 mm²/hr, 0.073 ± 0.081 mm²/hr and 0.13 ± 0.20 mm²/hr, respectively. The healing rate of the cornea in terms of the decrease in wound area (mm²/hr) was not significantly different among the three groups. (ANOVA: p = 0.64, 0.32, 0.65, 0.20 respectively)

The corneal healing rate in terms of the decrease in the wound radius (mm/hr) during post operative 0-1 day in the P, A and S groups were 0.18 ± 0.04 mm/hr, 0.14 ± 0.08 mm/hr and 0.17 ± 0.06 mm/hr, respectively. The corneal healing rate during post operative 1-2 day in the P, A and S groups were 0.28 ± 0.03 mm/hr, 0.31 ± 0.03 mm/hr and 0.28 ± 0.04 mm/hr, respectively. The corneal healing rate during post operative 2-3 day in P, A and S groups were 0.21 ± 0.03 mm/hr, 0.19 ± 0.04 mm/hr and 0.20 ± 0.05 mm/hr, respectively. The corneal healing rate during post operative 3-4 day in P, A and S groups were 0.05 ± 0.06 mm/hr, 0.06 ± 0.07 mm/hr and 0.07 ± 0.10 mm/hr, respectively. The healing rate of the cornea in terms of the decrease in the wound radius (mm/hr) was not significantly different among the three groups. (ANOVA: p = 0.47, 0.31, 0.65 and 0.92, respectively)

**DISCUSSION**

Jeffrey et al. found a strong positive correlation between the healing rates and the initial wound areas. The mean healing rate of the 8-mm diameter wounds (0.91 mm²/hr) was significantly greater than that of the 6.5-mm diameter wounds (0.80 mm²/hr). The 4-mm diameter wounds healed at a significantly slower rate (0.37 mm²/hr) when compared to the 6.5-mm diameter wounds. By comparison, regardless of the initial wound area, the wound diameter decreased at a rate of approximately 0.1 mm/hr, which may explain the dependency of the healing rate on the initial wound area. Craig et al. found that the decrease in wound area (mm²/hr) was neither linear nor amenable to simple kinetic analysis. However, analysis of the data in terms of the decrease in the wound radius (mm/hr) revealed a biphasic process consisting of an initial latent phase with no epithelial movement (5.5 ± 0.3 hr), followed by a linear healing phase. The rate of epithelial movement in the linear healing phase was 0.064 ± 0.002 mm/hr. Neither the latent phase nor the rate of epithelial migration during the healing phase was affected by variations in initial wound size (2.4-6 mm diameter).

There were two studies, to our knowledge, to document epithelial healing rates in human cornea. In one study, the average healing rate of nondiabetic patients was linear (17.8 ± 7.8 mm²/day, 0.57 ± 0.21 mm/hr) with an 8-mm diameter wound and a light patch. In the other study, the area of epithelial defects decreased exponentially with time, indicating a constant rate of epithelial migration with variable wound size and a pressure patch.

In the early phases (0-1 day) of healing in our study, there was a slow progression of epithelium compared with the later days. This might be due to 2 pharmacological actions of subtenon injected methylprednisolone and gentamycin, or this may involve the initial transformation of the epithelial cells into motile cells during the latent phase which is followed by a linear healing phase if measured by
the radius of defect. Furthermore, there may be some widening of epithelial wound through unintentional removal. This factor should be taken into account.

Less notable, but significant, delays were found in our study during the later phases of healing, however the long spacing between measurements (24 hours), necessary to limiting the disturbance of the contact lenses and lid closure, precluded the exact determination of the time of epithelial closure. This would tend to underestimate the differences in the later phases of epithelial healing.

Past studies on corneal wound healing in rabbits have shown that cell migration is present at 16 to 24 hours. This migration was inhibited by placing soft contact lenses containing 39% water with a low O2 transmissibility (8.9 × 10^{-10} DK/L) over the lesioned corneas. In that same study soft contact lenses containing 58% water with an O2 transmissibility (4.3 × 10^{-9} DK/L) did not inhibit movement. It is generally agreed that oxygen is the only metabolic requirement offered to the cornea from the tears, and that other nutrients are supplied by the aqueous humor and limbal blood vessels.

Disposable contact lenses are inexpensive hydrogel lenses approved for both daily and extended wear. The oxygen permeability values determined for each lens material in this study are as follows: Acuvue®, 18 × 10-11 cm2 ml O2/sec ml mm Hg (DK); and SeeSequence®, 9 × 10-11 Dk (Table 2). The oxygen permeability of these lenses may be high enough so as not to hinder the corneal epithelial healing.

The corneal epithelial healing rate during postoperative 1,2 and 3 days are 0.33, 0.78 and 0.44 mm²/hour in the pressure patch group; 0.24, 0.92 and 0.37 mm²/hour in the Acuvue® CL group; and 0.30, 0.79 and 0.38 mm²/hour in the SeeSequence® CL group. From the above results, it may be concluded that a disposable contact lens does not hinder epithelial healing compared with a pressure patch.

REFERENCES


EPITHELIAL HEALING TIME AND RATE