Stimulating Re-epithelialization After Photorefractive Keratectomy

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ABSTRACT

BACKGROUND: Re-epithelialization is usually complete in eyes 3 to 4 days following photorefractive keratectomy (PRK). However, this process is delayed in 0.5% of these eyes, leading to early development of haze. The authors investigated a method to stimulate re-epithelialization following PRK.

METHODS: PRK was performed with the Nidek EC-5000 excimer laser. Following surgery, express-cytokinotherapy was applied. This method consisted of a single subconjunctival injection of 2.5 to 3.0 ml of ex juvanticus mixture of autologous and immunomodulator Poludan. This mixture was then applied topically 4 times a day until re-epithelialization was complete. Poludan is an interferon inducer (complex polyA: polyU), stimulates expressed production of interferon and interleukin-2, and increases natural cytotoxicity.

RESULTS: Thirty eyes of 30 patients with delayed re-epithelialization were treated with the described method. The average time to re-epithelialization was 7.00 ± 0.64 days. Total epithelialization was complete on day 3 ± 0.38 after beginning the cytokinotherapy (P<0.05). Early haze developed in only 2 patients from this group. Occurrence of early haze in the control group of patients who had persistent epithelial defects 8 to 16 days postoperatively and were given traditional therapy including corticosteroid and non-steroidal drugs was reliably higher: 8 to 10 days (P<0.01).

CONCLUSION: Local express-cytokinotherapy appears to be an effective method to promote quick and complete epithelialization in eyes following PRK that experience delayed re-epithelialization.

This treatment may be an important part of the prevention of early haze development and achievement of better visual acuity. [J Refract Surg 1999;15(suppl):S234-S237]
postoperative treatment to stimulate re-epithelial-
ization following PRK in cases of delayed corneal
healing.

**PATIENTS AND METHODS**

Forty patients from 21 to 48 years old (mean, 30.5 yr) were included. These patients had corneal
epithelial defects ranging in size from 1.0 to 3.0 mm
following PRK with the Nidek EC-5000 excimer
laser. Patients were separated into three groups: 18
patients with myopia, 12 patients with hyperopia,
and 10 patients who served as a control group.

Epithelial defects and haze in both the epithelial
and subepithelial layers of the cornea have been
noted during the PRK postoperative period. The
intensity of the defect can be rated by the following
scale developed by the authors: a score of 0 indicates
a completely clean cornea as viewed with biomi-
croscopy, and a score of 1 to 3 indicates different lev-
els of opacity in the superficial layers of the ablation
zone.

An eye ointment consisting of a combination of
corticosteroids and antibiotics was administered
after PRK. The eyes were evaluated on the fourth
postoperative day. If re-epithelialization was incom-
plete in the treated myopic and hyperopic eyes, they
were treated by express autokinetotherapy. A mix-
ture of autoblood (6 ml) and immunomodulator
Poludan 0.5 ml, 100 U (Russia) was injected subcon-

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td><strong>Re-epithelialization, Haze, and Uncorrected Visual Acuity in 3 Groups of Eyes After PRK</strong></td>
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<tr>
<td>Uncorrected Visual Acuity at 1 mo</td>
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<tr>
<td><strong>Group 1 (Myopia)</strong></td>
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<tr>
<td>17 eyes (94.5%) healed in 4 to 5 days</td>
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<tr>
<td>1 eye (5.5%) healed in 6 days</td>
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<tr>
<td><strong>Group 2 (Hyperopia)</strong></td>
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<tr>
<td>9 eyes (75%) healed in 4 to 5 days</td>
</tr>
<tr>
<td>3 eyes (25%) healed in 6 days</td>
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<tr>
<td><strong>Group 3 (Control)</strong></td>
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<tr>
<td>2 eyes (20%) healed in 4 to 5 days</td>
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<tr>
<td>8 eyes (80%) healed in 6 days</td>
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Antibiotic instillation and solcoseryl gel were
administered to the control group after the fourth or
fifth day.

**RESULTS**

Patient examinations were performed regularly
until corneal re-epithelialization was complete, and
then at 1, 3, and 6 months and 1 year postopera-
tively. Uncorrected visual acuity and spectacle-cor-
rected visual acuity were measured and slit-lamp
examination was performed at these intervals. After
express autokinetotherapy application, complete
re-epithelialization of the cornea occurred in an
average of 3.00 + 0.38 days; the average duration of
defects before treatment was 6.50 + 0.83 days for the
myopic patients. Corneal haze in the myopic group
was graded 1.0 to 1.5, and uncorrected visual acuity
was 0.5 to 0.6 in 94.5% of cases 1 month postopera-
tively. The haze intensity decreased to grade 1.0 at 3
months and the average uncorrected visual acuity
was 0.85. From 6 months to 1 year postoperatively,
haze decreased in these eyes to grades of 0.0 to 1.0,
and average uncorrected visual acuity stayed at
0.85. Early haze, as a rule, was more intense within
the optical zone when an epithelial defect was pre-

tent.
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Table 2
Persistence of Corneal Epithelial Defect Before and After Treatment

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>Persistence of Defect Before Treatment (days)</th>
<th>Persistence of Defect After Treatment (days)</th>
<th>Statistical Significance (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (myopia)</td>
<td>18</td>
<td>6.5 ± 0.83</td>
<td>3.0 ± 0.38</td>
</tr>
<tr>
<td>Group 2 (hyperopia)</td>
<td>12</td>
<td>7.0 ± 0.64</td>
<td>4.2 ± 1.2</td>
</tr>
<tr>
<td>Group 3 (control)</td>
<td>10</td>
<td>7.5 ± 1.97</td>
<td>6.75 ± 1.3</td>
</tr>
</tbody>
</table>

re-epithelialization on the fifth day following express-autocytokinotherapy application. Grade 2 haze and uncorrected visual acuity of 0.3 to 0.4 was observed at 1 month postoperatively. At 3 months, the haze grade decreased to 1.5 and uncorrected visual acuity increased to 0.7. Six months following PRK and beyond, the haze level remained at grade 1 while uncorrected visual acuity decreased to 0.2 and residual myopia was 1.50 D.

For the hyperopic group, the duration of corneal epithelial defects before treatment was an average of 7.00 ± 0.64 days. Following express autocytokinotherapy application, complete re-epithelialization occurred in an average of 4.20 ± 1.20 days. A haze grade of less than 1.5 and uncorrected visual acuity of 0.5 and higher was observed in 75% of eyes at 1 month following PRK. At 3 months, the haze intensity reduced to grade 0.5 to 1.0 and remained stable through subsequent examinations. Average uncorrected visual acuity was 0.6 and higher. In 3 eyes (25%), re-epithelialization was complete by the sixth day. A haze grade of 1.5 and uncorrected visual acuity of 0.35 was observed at 1 month following PRK. At 3 months, the haze grade decreased to 1.0 and uncorrected visual acuity increased to 0.45. Haze intensity remained stable through subsequent examinations.

No allergic reactions occurred among the myopic or hyperopic patients as a result of express autocytokinotherapy.

Re-epithelialization occurred at 6.75 ± 1.30 days in the control group following solcoseryl gel application. Haze graded 1.5 to 2.0 and uncorrected visual acuity of 0.35 was observed 1 month following PRK. At 3 months postoperatively, haze decreased to a grade of 1.5 and uncorrected visual acuity remained stable, but residual myopia was noted for 8 of 10 patients. From 6 months to 1 year postoperatively, haze graded 1.0 to 1.5 was observed, as well as residual myopia (Tables 1,2).

DISCUSSION

Express-autocytokinotherapy in the myopic and hyperopic patients studied resulted in complete re-epithelialization in 3 to 4 days on average in 86.7% of subjects (n=26). Re-epithelialization occurred 5 to 6 days after the onset of treatment in 100% of these eyes. In the control group, re-epithelialization occurred in 4 to 5 days in 25% of patients, and in 7 to 9 days in 100%. Poludana biosynthetic polyribonucleic acid complex of polyadenil and polyuridin acids, which increase interferon production and strengthen natural cytokinotoxic activity of monocytes, T-lymphocytes, and interleukin I-II response, along with cytokines that possess immune-correcting properties and autofibronectin inherent in the blood is effective in promoting re-epithelialization. 15

This study demonstrates that express-autocytokinotherapy therapy promotes the healing process in the cornea and decreases the chance of early haze formation following PRK, leading to improved visual acuity without toxic reactions in the cornea.

REFERENCES