Alcohol- vs Hypertonic Saline–Assisted Laser-Assisted Subepithelial Keratectomy

Rossen Hazarbassanov, MD; Oded Ben-Haim, MD; David Varssano, MD; Aharon Grinbaum, MD; Igor Kaiserman, MD, MSc, MPA

Objective: To evaluate the predictability and safety of hypertonic saline (5% sodium chloride)–assisted laser-assisted subepithelial keratectomy (HS-LASEK) vs 20% alcohol–assisted LASEK (A-LASEK).

Setting: American Laser Medical Center, Rishon Le-Zion, Israel.

Methods: Fifty-two consecutive eyes (26 patients) were randomized to HS-LASEK (30 eyes) and A-LASEK (22 eyes) groups. The patients’ eyes were examined, refractioned, and photographed at 1 day, 5 days, 2 weeks, and 1 month postoperatively by a masked physician. Corneal topography and confocal examination were performed before and 1 month after surgery.

Main Outcome Measures: The predictability, accuracy, and visual recovery of HS-LASEK vs A-LASEK in the first postoperative month.

Results: The accuracy of HS-LASEK was similar and sometimes better than A-LASEK. Two weeks after surgery, 17 eyes (57%) in the HS-LASEK group and 10 eyes (46%) in the A-LASEK group were within ± 0.5 diopter of the intended refractive correction (P<.05). At all time points eyes in the HS-LASEK group had better best-corrected visual acuity than eyes in the A-LASEK group, although the uncorrected visual acuity was similar. Eighteen (61%) of the HS-LASEK–treated eyes and 12 (55%) of the A-LASEK–treated eyes had an epithelial defect after surgery. The HS-LASEK–treated eyes had significantly larger epithelial defects. The resolution of the defects was faster in the HS-LASEK–treated eyes (mean±SD, 4.5±0.4 days vs 5.8±0.2 days, P=.002). The subepithelial scar was thicker in A-LASEK–treated eyes.

Conclusions: Hypertonic saline–assisted LASEK provides good postoperative accuracy, safety, and a similar rate of complications. In view of recent evidence regarding the epithelial toxic effects of alcohol, HS-LASEK might be a better treatment alternative.


Initially described by Azar et al1 and Camellin and Cimberle,2 laser-assisted subepithelial keratectomy (LASEK) is an alternative to photorefractive keratectomy (PRK) or to laser in situ keratomileusis (LASIK).3-5 In contrast with PRK that requires epithelial debridement, in LASEK an epithelial flap is created and repositioned after the anterior stromal ablation. This epithelial coverage is intended to inhibit the pronounced wound-healing response seen after PRK at the epithelial-stromal junction. Preliminary reports showed that LASEK is as safe and effective as PRK and LASIK and might be associated with less pain, haze, and a faster visual rehabilitation than PRK,6-9 although not all studies found such an advantage.10 Similarly to PRK, since LASEK is performed on the anterior cornea, there are virtually no flap- or interface-related complications per se. To create the epithelial flap, 20% alcohol is usually applied to the cornea for 25 to 35 seconds to loosen the anchoring structures of the epithelium. Some surgeons even apply the alcohol for 40 seconds claiming that they are unable to get a good epithelial flap with durations of shorter than 40 seconds. However, it was shown that after a 45-second exposure to 20% alcohol only half of the epithelial cells remain vital while longer exposure times (60 seconds and 120 seconds) showed predominantly dead epithelial cells.11 Chen et al12 applied 10% to 70% alcohol to immortalized human corneal epithelium for periods of 20 to 45 seconds, showing that the percentage of viable cells drops from 70% at a 30-second exposure to 20% alcohol only half of the epithelial cells remain vital while longer exposure times (60 seconds and 120 seconds) showed predominantly dead epithelial cells.11 Similarly to PRK, since LASEK is performed on the anterior cornea, there are virtually no flap- or interface-related complications per se.
vital at the time of repositioning, we attempted to replace the use of alcohol with a hypertonic saline (5% sodium chloride) (HS) solution. We compared the 2 methods from the applicability viewpoint, the accuracy of refractive correction, the final visual outcome, and the induced corneal damage during the first postoperative month.

METHODS

The study included 52 consecutive eyes (26 patients) treated with LASEK by 1 of us (O.B.H.). Thirty eyes were randomly treated with HS-assisted LASEK (HS-LASEK), while 22 eyes were treated with the conventional technique of alcohol-assisted LASEK (A-LASEK). Patients were offered the choices to either randomly receive 1 of the treatments in both eyes or to receive 1 of the treatments in one eye and the other treatment in the other eye (randomly assigned). Ten of the patients agreed to have 1 eye each randomized to receive HS-LASEK while the fellow eye underwent A-LASEK. The other 16 patients randomly received either of the treatments in both eyes (10 patients received HS-LASEK and 8 patients were randomized to receive A-LASEK, but 2 of them later refused to be included in the study). The patients were unaware of the type of procedure they received. The study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board of the American Laser Medical Center, Rishon Le-Zion, Israel. All participants signed an informed consent form.

Preoperative evaluation included ocular and general health histories, subjective refraction, corneal topography, corneal pachymetry, pupil size, cycloplegic refraction, and an ocular health examination. Patients who wore soft contact lenses were excluded from the study. All participants were without active infection at the time of repositioning, we attempted to replace the use of alcohol with a hypertonic saline (5% sodium chloride) (HS) solution. We compared the 2 methods from the applicability viewpoint, the accuracy of refractive correction, the final visual outcome, and the induced corneal damage during the first postoperative month.

Table 1. Preoperative Characteristics of the HS-LASEK vs the A-LASEK Group

<table>
<thead>
<tr>
<th>Factor</th>
<th>HS-LASEK (Range)</th>
<th>A-LASEK (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCVA</td>
<td>0.37 ± 0.21 (0.04 to 0.50)</td>
<td>0.31 ± 0.27 (0.03 to 0.67)</td>
</tr>
<tr>
<td>BCVA</td>
<td>0.96 ± 0.15 (0.67 to 1.0)</td>
<td>0.91 ± 0.19 (0.4 to 1.0)</td>
</tr>
<tr>
<td>Spherical equivalent, D</td>
<td>−5.8 ± 2.3 (−7.25 to −8.25)</td>
<td>−6.3 ± 3.1 (−3.5 to −9.37)</td>
</tr>
<tr>
<td>Sphere, D</td>
<td>−5.3 ± 2.5 (0.25 to 8.75)</td>
<td>−5.5 ± 2.9 (4.5 to 10.0)</td>
</tr>
<tr>
<td>Cylinder, D</td>
<td>−1.1 ± 0.8 (0.5 to 3.5)</td>
<td>−1.6 ± 0.8 (0.5 to 4.5)</td>
</tr>
</tbody>
</table>

Abbreviations: A-LASEK, 20% alcohol-assisted laser-assisted subepithelial keratectomy; BCVA, best-corrected visual acuity; D, dioptr; HS-LASEK, hypertonic saline (5% sodium chloride)–assisted LASEK; UCVA, uncorrected visual acuity.

*Data are given as mean ± SD. There was no statistically significant differences.

Figure 1. Achieved refractive correction vs attempted correction after 2 types of laser-assisted subepithelial keratectomy (LASEK). The periods of measurement are as follows: 2 weeks (A) and 1 month (B) after hypertonic saline (5% sodium chloride)–assisted LASEK (HS-LASEK) and 20% alcohol-assisted LASEK (A-LASEK). Dotted lines mark the ± 1-diopter (D) deviation. C, The mean (± SE) absolute deviation from attempted correction. Asterisks indicate *P < .05 by t-test.
anced salt solution (Aqsia, Chauvin Opsia SA; Laboratory of Coordination Chemistry, Toulouse, France) was used 3 to 4 times during the peeling to moisturize the epithelial surface. The denuded corneal surface was then ablated with an excimer laser (WaveLight-Allegretto scanning-spot laser; WaveLight Laser Technologie AG, Erlangen, Germany). Thereafter, the entire cornea was flooded with chilled balanced salt solution for 5 seconds and the flap was gently repositioned over the central cornea with a blunt tipped spatula (Sloane Flap Repositor; Katena Products Inc). A therapeutic, +0.25-power, soft contact lens (Carl Zeiss Optical, Inc, Chester, Va) was placed on the cornea.

A combination of 3 mg/mL of lomefloxacin hydrochloride 4 times daily, 0.1% of dexamethasone phosphate disodium 3 times daily, 0.1% diclofenac sodium 3 times daily, and 50 mg/mL of preservative-free povidone (Polyvidone) drops every hour were used for 5 days after undergoing LASEK. The soft contact lens was removed once there was no epithelial defect. Lomefloxacin, dexamethasone, and lubrication were continued for another week. Patients were clinically examined; their eyes were refracted and photographed at 1 day, 5 days, 2 weeks, and 1 month postoperatively, or more frequently when necessary, by a masked physician who was not aware of the type of procedure the patient underwent. When a corneal epithelial defect was present, its largest diameter was documented (if a contact lens was present, it was temporarily moved aside). One month after surgery corneal topography (Oculus; Oculus Optikgeräte GmbH, Wetzlar, Germany) and a corneal confocal examination (Confoscan 2 confocal microscope Navis version 3.4.1; Nidek Technologies, Vigonza, Italy) were performed. Continuous variables were compared using the \( t \) test. A difference was considered statistically significant at the \( P < .05 \) significance level.

### RESULTS

Thirty eyes of 20 patients (mean±SD age, 32.3±10.2 years) were assigned to the HS-LASEK group and 22 eyes of 16 patients (30.6±9.1 years) were treated with A-LASEK. The preoperative patients factors were similar in both groups (Table 1). All patients had stable refractions for at least 18 months; none had undergone previous refractive surgery. Eight eyes (4 in the HS-LASEK group and 4 in the A-LASEK group) developed “button-

<table>
<thead>
<tr>
<th>Deviation From Intended Correction, D</th>
<th>HS-LASEK Group 2 wk†</th>
<th>1 mo</th>
<th>A-LASEK Group 2 wk†</th>
<th>1 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>±0.5</td>
<td>56.7</td>
<td>70.0</td>
<td>45.5</td>
<td>68.2</td>
</tr>
<tr>
<td>±1</td>
<td>100.0</td>
<td>100.0</td>
<td>77.3</td>
<td>99.9</td>
</tr>
<tr>
<td>±2</td>
<td>NA</td>
<td>NA</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Abbreviations: A-LASEK, 20% alcohol–assisted laser-assisted subepithelial keratectomy; D, dioptr; HS-LASEK, hypertonic saline (5% sodium chloride)–assisted LASEK; NA, not applicable.

*Data are given as percentages.
†P < .05 by \( t \) test.

<table>
<thead>
<tr>
<th>VA</th>
<th>Preoperative BCVA</th>
<th>1 mo After LASEK</th>
</tr>
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<tbody>
<tr>
<td>≥20/15</td>
<td>0</td>
<td>6.6</td>
</tr>
<tr>
<td>≥20/20</td>
<td>83.3</td>
<td>89.0</td>
</tr>
<tr>
<td>≥20/25</td>
<td>93.3</td>
<td>100.0</td>
</tr>
<tr>
<td>≥20/40</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Abbreviations: A-LASEK, 20% alcohol–assisted laser-assisted subepithelial keratectomy; BCVA, best-corrected visual acuity; HS-LASEK, hypertonic saline (5% sodium chloride)–assisted LASEK; UCVA, uncorrected visual acuity; VA, visual acuity.

*Data are given as percentages.
†Four patients in the HS-LASEK group and 5 patients in the A-LASEK group had requested undercorrection for monovision. Those patients were excluded from the UCVA calculations.
holes” during lifting of the epithelial flap, but these did not seem to delay healing.

In 5 A-LASEK–treated eyes (22.7%) the alcohol treatment had to be repeated for 10 to 15 additional seconds, as the surgeon could not easily peel the epithelial flap. This did not seem to affect the outcome compared with the other A-LASEK–treated eyes. No such cases occurred in the HS-LASEK–treated eyes. The lifting of the epithelial flap in the HS-LASEK–treated eyes was easier, although it did sometimes result in buttonholes. In both groups corneal epithelial defects developed in several patients. No other serious flap complications occurred in either group and no procedures had to be discontinued. No obvious difference was noted between the 2 groups for postoperative pain or discomfort. There have been no long-term epithelial problems such as recurrent erosions and no severe dry eye problems. No patient required punctal occlusion.

**Figure 1** shows the achieved refractive correction (spherical equivalent) vs the attempted refractive correction 2 weeks (Figure 1A) and 1 month (Figure 1B) after LASEK in both groups. It also shows the mean deviation of the achieved refractive correction from the attempted refractive correction (Figure 1C). While this deviation was always smaller in the HS-LASEK–treated eyes, the difference between the groups was statistically significant at 2 weeks (P<.04, t test) and lost its statistical significance 1 month after LASEK (P=.50, t test).

**Figure 2** shows the geometric mean (calculated in logarithm of the minimum angle of resolution [LogMAR] units) of the best-corrected (BCVA) and the uncorrected (UCVA) visual acuity in each group during the first postoperative month. The UCVA calculations do not include eyes that were intentionally undercorrected for reading (monovision). At all time points the HS-LASEK–treated eyes had a better mean BCVA than the A-LASEK–treated eyes. The difference between the groups was statistically significant at 2 weeks (P<.01, t test), 5 days (P=.03, t test) and 1 month (P=.03, t test) postoperatively. There was no difference in the UCVA at any time point. **Table 3** lists the BCVA and UCVA distribution 1 month after LASEK.

When a corneal epithelial defect (erosion) was present, we followed it up to its resolution, each time measuring its largest diameter. Eighteen (60%) of the HS-LASEK–treated eyes and 12 (55%) of the A-LASEK–treated eyes had an epithelial defect 1 day after surgery. After 5 days a faint opaque line was noted in the central portion of the epithelium in 18 (60%) of the HS-LASEK–treated eyes and in 18 (82%) of the A-LASEK–treated eyes.

**Figure 3** shows the distribution of the erosion diameter at 1 (Figure 3A) and 5 days (Figure 3B) postoperatively and the changes in the mean diameter during follow-up (Figure 3C). Both at 1 and 5 days postoperatively the HS-LASEK–treated eyes had a larger mean corneal epithelial defect. The difference in the mean±SD erosion diameter was statistically significant at 1 day postoperatively (4.0±0.8 mm in the HS-LASEK–treated eyes vs 2.5±0.5 mm in the A-LASEK–treated eyes, P=.03, t test) but not later. In either group there was no corneal epithelial defect 2 weeks after LASEK. The mean±SD time to resolution of the epithelial defect was 4.5±0.4 days in the HS-LASEK–treated eyes and 3.8±0.2 days in the A-LASEK–treated eyes (P=.002, t test). Removal of the soft contact lens from the treated eye was dependent on the epithelial status. In HS-LASEK–treated eyes the contact lens was removed after a mean±SD of 5.1±0.2 days and in the A-LASEK–treated eyes after 5.9±0.2 days (P=.001, t test).

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**Table 1**

<table>
<thead>
<tr>
<th>Time After LASEK Treatment</th>
<th>A-LASEK Group</th>
<th>HS-LASEK Group</th>
</tr>
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<tbody>
<tr>
<td>1 day</td>
<td>20 (82%)</td>
<td>18 (60%)</td>
</tr>
<tr>
<td>5 days</td>
<td>12 (55%)</td>
<td>18 (60%)</td>
</tr>
<tr>
<td>2 weeks</td>
<td>12 (48%)</td>
<td>18 (60%)</td>
</tr>
<tr>
<td>1 month</td>
<td>18 (82%)</td>
<td>18 (60%)</td>
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</table>

**Table 2**

<table>
<thead>
<tr>
<th>Time After LASEK Treatment</th>
<th>HS-LASEK Group</th>
<th>A-LASEK Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 day</td>
<td>4.0±0.8 mm</td>
<td>2.5±0.5 mm</td>
</tr>
<tr>
<td>5 days</td>
<td>3.8±0.2 mm</td>
<td>2.5±0.5 mm</td>
</tr>
<tr>
<td>2 weeks</td>
<td>3.8±0.2 mm</td>
<td>2.5±0.5 mm</td>
</tr>
<tr>
<td>1 month</td>
<td>3.8±0.2 mm</td>
<td>2.5±0.5 mm</td>
</tr>
</tbody>
</table>

**Table 3**

<table>
<thead>
<tr>
<th>BCVA Distribution 1 month after LASEK</th>
<th>0</th>
<th>0-1</th>
<th>1-2</th>
<th>2-3</th>
<th>3-4</th>
<th>4-5</th>
<th>5-6</th>
<th>&gt;7</th>
</tr>
</thead>
<tbody>
<tr>
<td>HS-LASEK Group</td>
<td>20 (82%)</td>
<td>18 (60%)</td>
<td>12 (55%)</td>
<td>18 (60%)</td>
<td>18 (82%)</td>
<td>18 (60%)</td>
<td>18 (82%)</td>
<td>18 (82%)</td>
</tr>
<tr>
<td>A-LASEK Group</td>
<td>12 (55%)</td>
<td>12 (55%)</td>
<td>12 (55%)</td>
<td>12 (55%)</td>
<td>18 (82%)</td>
<td>18 (82%)</td>
<td>18 (82%)</td>
<td>18 (82%)</td>
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</table>
Figure 4 shows a confocal examination performed 1 month after surgery in a patient who had A-LASEK in the right eye (Figure 4A-D) and HS-LASEK in the left eye (Figure 4E-H). No differences were noted between the 2 groups in any of the patients regarding corneal epithelium (Figure 4A and E), stromal keratocytes (Figure 4C and G), or endothelial cell count (Figure 4H). In the A-LASEK–treated eyes the mean±SD endothelial cell count was 2552±325 cells/mm² while in the HS-LASEK–treated eyes, it was 2616±372 cells/mm². We noticed a difference in the mean±SD thickness of the subepithelial scar that was 45.8±12.8 µm in the HS-LASEK–treated eyes and 63.5±9.1 µm in the A-LASEK–treated eyes (P<.001, t test). As can be seen in Figures 4B and F the subepithelial scar looks denser in the A-LASEK–treated eyes.

COMMENT

Laser-assisted subepithelial keratectomy seems to be a blend of the positive aspects of PRK and LASIK, while reducing some of the complications inherent in both procedures. Its advantages include rapid visual recovery, good final UCVA, minimal pain and haze, conservation of corneal stroma, and good refractive stability. Moreover, some LASIK complications such as poorly created or wrinkled flaps, flap dislocation, dry eyes, difficulty predicting flap thickness, corneal ectasia, epithelial ingrowth, and diffuse lamellar keratitis are absent in LASEK.

The LASEK technique described by Camellin and Cimberle calls for a 20% alcohol solution to be applied to the epithelium for 20 seconds, to weaken its attachment to the Bowman membrane, allowing the removal of a continuous layer of tissue. Gabler et al showed that exposure to 20% alcohol should be limited to less than 30 seconds as the number of vital epithelial cells rapidly decreased thereafter. Moreover, alcohol can leak out from the holding well and damage conjunctival epithelial cells that were not meant to be affected. Thus, alcohol seems to be a blessing in disguise, as too long of an application can damage the epithelial cells and too short of an ap-
application does not suffice to detach the flap. Recently, McDonald\textsuperscript{22} proposed to use 0.3% hydroxypropyl cellulose gel rather than alcohol to loosen the epithelium. This new technique requires the development of new instruments, including perforated cannulas and usage of a suction ring. We have been able to lift the epithelial flap using a 5% sodium chloride solution without the need for any new instrument.

Claringbold\textsuperscript{3} has reported that in 16.7% of patients the alcohol treatment had to be repeated to facilitate epithelial peeling. We also encountered such events in about 18% (4/22) of the A-LASEK–treated eyes but in none of the HS-LASEK–treated eyes. Although there were buttonholes created in both groups, we felt that the HS-LASEK–treated flap was easier to lift. The advantages of HS-LASEK seem to be more prominent in the immediate postoperative period when both the accuracy of refractive correction and the BCVA seem to be better than in the A-LASEK–treated eyes. This may be the result of less damage to the corneal epithelium leading to less epithelial regeneration, less epithelial edema, and less scar formation (as we noted in the confocal studies).

In this study HS-LASEK induced a larger epithelial defect than A-LASEK. However, this epithelium seems to be more viable resulting in a shorter time of healing (4.5 days vs 5.8 days, respectively). These results could be biased by the methods of measuring the epithelial defect that involved moving the contact lens. This could delay wound healing as the epithelium tends to stick to it, although it should not favor any of the groups. It is also conceivable that an optimization of the HS-LASEK method in the future might result in smaller epithelial defects.

Camellin and Cimberle\textsuperscript{2} reported that 90% of patients who underwent LASEK were able to regain 80% of their preoperative BCVA in fewer than 10 days. Azar et al\textsuperscript{11} reported a UCVA of 20/25 or more at 1 month after LASEK in 92% of the eyes. Our results are similar as 100% (30/30) of HS-LASEK–treated eyes and 96% (21/22) of the A-LASEK–treated eyes had a BCVA of 20/25 or more 1 month after LASEK and more than 90% (47/52) in both groups had a UCVA of 20/25 or more. Azar et al also reported a refractive correction accuracy of ± 0.5 (D) in 58% (7/12) of the eyes at 1 month. We also found an accuracy of ± 0.5D in about 15 (68%) of the A-LASEK–treated eyes and a better result of about 21 (70.0%) in the HS-LASEK eyes.

Thus, we have shown that HS-LASEK is similar to, or better than, A-LASEK for predictability, safety, and postoperative recuperation for up to 1 month. A future study of HS-LASEK's effect on epithelial cell vitality would be most interesting. As wavefront-based ablation outcomes are often better with PRK than with LASIK,\textsuperscript{23} the application of LASEK, as an improved method of PRK, is expected to rise. A more epithelium-friendly method of flap creation might be warranted.

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Acknowledgment: Drs Hazarbassanov and Kaiserman equally contributed to this work.

REFERENCES

cal intervention has the potential to significantly reduce patient suffering resulting from strabismus.

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Correspondence: David K. Coats, MD, Department of Ophthalmology, Baylor College of Medicine and the Texas Children’s Hospital, 6621 Fannin, MC640.00, Houston, TX 77030 (dcoats@bcm.tmc.edu).

REFERENCES


Correction

Incorrect Dilution of Sodium Chloride. In the article by Hazarbassanov et al titled “Alcohol- vs Hypertonic Saline–Assisted Laser-Assisted Subepithelial Keratectomy,” published in the February issue of the Archives (2005;123:171-176), the percentage of sodium chloride should have been 5% throughout the article. The journal apologizes for the error.