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Laser-assisted subepithelial keratectomy (LASEK) without alcohol versus photorefractive keratectomy (PRK)

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PURPOSE. *To evaluate epithelial healing and visual outcome after laser-assisted subepithelial keratectomy (LASEK) without alcohol de-epithelialization and to compare this technique to photorefractive keratectomy (PRK) in myopia.*

METHODS. *In a series of 1953 patients undergoing bilateral myopic PRK, an epithelial flap could be obtained by manual de-epithelialization in the left eye of 56 patients without alcohol exposure. The right eye was treated by PRK and the left by LASEK (i.e., repositioning the viable flap after surface ablation). The two eyes were compared in terms of pain, uncorrected visual acuity (UCVA) in decimals, correction achieved, and haze. The epithelial healing pattern was assessed in the LASEK eyes.*

RESULTS. *The flap remained viable, showing a peripheral junction, in 25 eyes (45%). Pain was higher in the PRK eye in 11/56 patients (20%), higher in the LASEK eye in 23/56 patients (41%), and the same in both eyes in 22/56 patients (39%). UCVA at one week was slightly better in the LASEK eyes (median 0.7 versus 0.6, p=0.002 with Wilcoxon test), but was the same in PRK and LASEK eyes after 1 month (median 0.9 in both). Median haze at 6 months was 0.5 in the PRK eyes and 0 in the LASEK eyes (Wilcoxon p=0.007). Median postoperative defocus equivalent at 9 months was 0.5 diopters in both the PRK and the LASEK eyes.*

CONCLUSION. *Although our study might have selected patients with loose epithelium, LASEK performed by manual de-epithelialization in the absence of alcohol exposure is not less painful than PRK, even in case of flap survival. Visual recovery speed, as well as haze, is slightly better than in PRK, although the difference is clinically negligible. (Eur J Ophthalmol 2003; 13: 676-80)*

KEY WORDS. *Haze, Laser-assisted subepithelial keratectomy (LASEK), Photorefractive keratectomy (PRK)*

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INTRODUCTION

Laser-assisted subepithelial keratectomy (LASEK) has recently been proposed as an alternative to photorefractive keratectomy (PRK) for the correction of ametropias by excimer laser (1-6). This technique is based upon the detachment of an epithelial flap after a 20- to 30-second application of an 18 to 20% alcohol solution, excimer laser ablation, and final reposition of the epithelial flap. Its theoretical advantages over PRK are reduced pain, reduced haze, and faster visual recovery, but the few comparative studies on small series published to date show conflicting results. In 27 patients treated by PRK in one eye and LASEK

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in the other, lower pain and haze were found with LASEK (7), whereas in a similar study of 25 patients, LASEK was characterized by more discomfort, and recovery speed did not differ between PRK and LASEK (8). In a third study, LASEK caused less haze and less pain than PRK, but no bandage contact lens (which is the rule after PRK) was used in either case (9).

Damage to corneal epithelial cells after diluted alcohol exposure is dose- and time-dependent (10, 11), and may affect healing speed and pain after LASEK. Devices such as microkeratomes to perform LASEK without alcohol are under investigation (12) . However, clinical results of LASEK without alcohol exposure have not been studied, owing to the lack of alternative methods of de-epithelialization.

In 4.6% of PRK candidates (according to the current series), manual removal of an uninterrupted epithelial flap can be achieved by a spatula, without alcohol exposure. We report a prospective study of patients receiving PRK in one eye and LASEK without alcohol in the fellow eye, comparing pain, speed of visual recovery, haze, and epithelial healing pattern. Although such a technique might select patients with loose epithelium, the purpose of the study is to evaluate LASEK without the interference of alcohol, assessing whether and how LASEK substantially differs from PRK. The study required a large number of eligible patients in order to obtain a sufficient series of epithelial flaps without alcohol exposure.

PATIENTS AND METHODS

This prospective, paired-eye, nonrandomized, single-surgeon study was performed on a population of 1953 patients undergoing same-day bilateral myopic PRK between April 2000 and January 2002. The study was approved by the ethical committee of our institute.

All patients provided informed consent. Preoperative exclusion criteria were diabetes, collagen disorders, corneal pathologies (including keratoconus, epithelial and stromal abnormalities, and history of recurrent erosions), previous corneal surgery, difference of more than 2 diopters (D) of spherical equivalent between the two eyes, and astigmatism greater than 2.5 D. Preoperative evaluation included manifest and cycloplegic refraction, uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), slit-lamp and fundus examination, tonometry, computed videokeratography, pupillometry, and ultrasound central pachymetry.

Sixty and 30 minutes before operation, ciprofloxacin 0.3% eyedrops (Ciloxan) were administered. Topical anesthesia consisted of one drop of proparacaine 0.5% (Alcaine) 10 and 5 minutes prior to surgery. The right eye was treated first with manual debridement of the corneal epithelium for a diameter of 9 mm; then PRK was performed with the Bausch & Lomb 217c excimer laser, in Planoscan mode. Chilled balanced salt solution (BSS) was then dripped onto the stromal bed.

If a loose and easily removable epithelium was encountered in the right eye, the left eye was then treated with LASEK as follows: a 9 mm 270° blunt epithelial trephine (Rhein 8-17014) was pressed on the cornea and rotated 10° to cut through the epithelium, leaving a superior hinge. A microhue (Rhein 8-17018) was used to elevate the flap edge; then the epithelial flap was detached with a spatula (Rhein 8-17017) and collected superiorly. A flap protector (Katena K3-1770) was used to cover the flap while laser ablation was performed (Bausch & Lomb 217c excimer laser, in Planoscan mode). Chilled BSS was then dripped onto the stromal bed, which was finally covered with the epithelial flap by a smooth spatula (Rhein 8-17019), approximating the flap edges to the originally trephined margins. A Weck-Cel sponge (Solan Ophthalmic Products) was used to gently paint and dry the flap, in order to make it adhere.

Intraoperative exclusion criteria were imperfect epithelial flap (tear, irregular margins, or buttonhole), laser damage to the flap, and missed adhesion of flap to stromal bed. In such cases, the epithelial flap was removed, and the procedure was converted to PRK.

At the end of both PRK and LASEK, a Soflens 66 F/M +0.5 D soft contact lens (Bausch & Lomb) was applied to the eye. Ciprofloxacin eyedrops and diclofenac unpreserved eyedrops (Voltaren) were instilled, and flap and lens were checked at the slit lamp. Postoperative medications consisted of topical ciprofloxacin five times a day for the first week, topical diclofenac four times a day for 2 days, and unpreserved hyaluronic acid eyedrops (Hyalistil) as artificial tears four to six times a day. Patients were instructed to use the same amount of eyedrops in both eyes. Follow-up visits were at days 1, 3, 5, 7, and 30, and months 2, 4, 6, 9, and 12. The contact lens was removed when epithelialization was complete (usual-

ly day 5 to 7), and fluorometholone eyedrops (Flarex) were started three times a day for the first month, and then tapered if the refraction was within 0.5 D, and stopped if overcorrection was found at one month.

Postoperative exclusion criteria were movable flap under the contact lens, loss of the bandage contact lens in either eye, infection, or noncompliance to medical treatment or to follow-up visits.

Randomization was not possible owing to the peculiarity of the study, in which only a small percentage of the initial candidates completed the procedure. Patients estimated pain in a written questionnaire, in which they were asked whether they had experienced more pain or discomfort in the right eye or in the left eye, or if pain/discomfort was the same in both eyes. Visual acuity was measured by a technician who was not aware of the study, could not observe the patient at the slit lamp, and did not know whether the patient had undergone PRK or LASEK in the left eye.

Haze was graded as follows: grade 0 = clear at the slit lamp; grade 0.5 = trace, barely visible at the slit lamp with indirect, broad, tangential illumination; grade 1 = minimal haze, seen with difficulty with direct and diffuse illumination; grade 2 = mild haze easily visible with direct focal slit illumination (13). No haze greater than grade 2 was observed.

Epithelial healing pattern after LASEK was assessed at the slit lamp, observing whether the epithelium had completely regrown as in PRK, with a central irregular junction (pattern C) or a U-shaped junction at the margins created by trephination (pattern U).

Statistical analysis was performed by StatView (Abacus Concepts, Inc., Berkeley, CA) and 95% confidence intervals (CI) calculated by CIA software (14). P values less than 0.05 were considered statistically significant.

RESULTS

Table I shows the participation data of all recruited patients. The mean age of final participants (56 patients) was 37 years (standard deviation (SD) 9.6; range 25 to 56). Twenty-three were men (41%). Eight were contact lens wearers (14%).

Epithelial healing pattern in LASEK eyes

In 31 eyes (55%; CI = 42% to 67%), a C pattern was observed. In the remaining 25 (45%), the junction had a U shape (U pattern). No correlation was found between age, sex, previous contact lens wear, and healing pattern.

Pain

Pain was higher in the PRK eye in 11/56 patients (20%), in the LASEK eye in 23/56 patients (41%), and the same in both eyes in 22/56 patients (39%). Excluding the 22 neutral patients, the LASEK eyes were significantly more painful (23/34, corresponding to 68%, with CI = 51% to 81%).

No correlation between pain and epithelial healing pattern was observed: with U pattern, more pain was

TABLE I - PARTICIPATION DATA OF ALL RECRUITED PATIENTS UNDERGOING BILATERAL MYOPIC EXCIMER LASER ABLATION

Inclusion and exclusion criteria	Number of participants	Percent of population
Eligible participants with informed consent	1953	100.0
Excluding patients with corneal pathologies or previous corneal surgery	1882	96.3
Excluding patients with eyes differing more than 2 D of spherical equivalent	1425	73.0
Excluding patients with astigmatism >2.5 D	1207	61.8
Patients where an epithelial flap was obtained	89	4.6
Excluding patients with damaged or unstable flap	65	3.3
Excluding patients having lost a contact lens (any eye)	58	3.0
Excluding patients noncompliant (final number of participants)	56	2.9

D = Diopters

felt in the PRK eye in 6/18 eyes (33%); with C pattern, more pain was felt in the PRK eye in 5/16 eyes (31%); CI for the difference: -28% to 30%.

Visual recovery speed

Visual recovery speed was measured by UCVA in decimals at one week. In the PRK eye, the median was 0.6 (75 and 25 percentiles: 0.7 and 0.5). In the LASEK eye, the median was 0.7 (75 and 25 percentiles: 0.8 and 0.6). Comparison by Wilcoxon paired data test gave a z-value of -3.14, with p=0.002.

UCVA at one week was also considered comparing LASEK eyes with C-pattern healing versus LASEK eyes with U-pattern, to assess whether the latter accelerated visual recovery. In the C group, the median UCVA was 0.7; in the U group, it was 0.8 (CI 0 to 2).

Visual acuity at one month did not differ significantly between PRK and LASEK eyes. In the PRK eyes, the median was 0.9 (75 and 25 percentiles: 1.0 and 0.8); in the LASEK eyes, the median was 0.9 (75 and 25 percentiles: 1.0 and 0.75). Comparison by Wilcoxon paired data test gave a z-value of -0.41, with p=0.68.

Haze

Low haze levels were measured in both eyes at six months. In the PRK eyes, the median was 0.5 (75 and 25 percentiles: 0.5 and 0). In the LASEK eyes, the median was 0 (75 and 25 percentiles: 0.5 and 0). Comparison by Wilcoxon paired data test gave a z-value of -2.69, with p=0.007.

Achieved correction

Achieved correction was evaluated in terms of defocus equivalent (DEQ), calculated as the sum of the spherical equivalent magnitude plus half the cylinder magnitude (15). Preoperative data were the same in the PRK and LASEK eyes, with a median of 3 D (75 and 25 percentiles: 6 and 2 D).

Postoperative DEQ at 9 months was as follows: in PRK eyes, the median was 0.5 D (75 and 25 percentiles: 0.5 and 0). In LASEK eyes, the median was 0.5 D (75 and 25 percentiles: 0.65 and 0.6). Comparison by Wilcoxon paired data test gave a z-value of -0.71, with p=0.78.

DISCUSSION

Our data show that LASEK performed by manual de-epithelialization in the absence of alcohol exposure is not associated with reduced pain when compared to PRK. In agreement with a previous study where alcohol was used (8), LASEK caused more discomfort.

Two types of epithelial healing can be identified: the former (pattern C in our study) is characterized, as in PRK (16), by epithelial cell migration and division to fill the epithelial defect, and is clinically evident as an irregular junction line in the center of the cornea. The latter (pattern U in our study) is peculiar to LASEK, occurring in approximately half of the cases, and characterized by survival of the epithelial flap, with a junction corresponding to the trephination line. We found that both patterns are associated with more pain than PRK.

Visual recovery is faster in LASEK, especially with U pattern, but statistical significance does not necessarily mean a clinical advantage, and rather than the bare p value, the small UCVA difference at 1 week (0.1) between PRK- and LASEK-treated eyes should be noted. In both PRK and LASEK, a good final visual acuity and correction were observed.

Weaknesses of the study are as follows: 1) lack of randomization, and LASEK always being performed on the left eye (owing to the impossibility of upsetting operating staff routine for such a large number of eligible patients); 2) different surface smoothness after manual de-epithelialization compared with alcohol de-epithelialization as in standard LASEK (17); 3) LASEK performed in a population mainly composed of non–contact lens wearers, who might have a peculiar healing pattern; and 4) patients in whom manual de-epithelialization was possible may represent a subgroup of eyes with loose epithelium and healing problems, which may affect results in both LASEK and PRK eyes, and may bias comparison with other studies (7-9). As for the first point, we tried to reduce bias by using a written questionnaire for pain and a single-masked visual acuity assessment; it has been impossible, however, to mask slit lamp haze evaluation.

In previous studies comparing LASEK with PRK, epithelial healing pattern was not specified (7, 8); therefore, it is difficult to understand whether different outcomes may have reflected different percentages of pattern C and U healers. The issue of flap survival has not been specifically evaluated in most clinical

studies on LASEK (1-6), except for an article reporting epithelial defects in 63% of cases at day 1 (18), and another article stating that all flaps survived (9). Better flap survival and reduced discomfort in LASEK have been reported with removal of a thin paracentral epithelial line, and alcohol exposure followed by retraction of the two opposite epithelial flaps ("butterfly" LASEK), which are left connected to the limbus (instead of trephination) (19).

In conclusion, alcohol avoidance in LASEK did not ensure flap survival, which occurred in only 45% of eyes, although our study might have selected patients with loose epithelium. LASEK performed by manual de-epithelialization in the absence of alcohol exposure is not less painful than PRK, even in case of flap survival. However, visual recovery speed and haze are slightly better than in PRK, although the difference is clinically negligible. Understanding of healing mechanisms and evaluation of haze and regression on higher myopias are needed.

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