The Effect of Cyclosporine A (Restasis) on Recovery of Visual Acuity Following LASIK

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ABSTRACT

PURPOSE: To compare the recovery of uncorrected visual acuity (UCVA) following LASIK in patients treated with topical cyclosporine A 0.05% and patients treated with a standard postoperative regimen.

METHODS: In this single-center, open-label, retrospective study, a standard refractive workup was performed in 45 patients (85 eyes) who underwent LASIK and did not have preexisting dry eye. In 36 eyes, a standard postoperative eye drop regimen was followed, and in 49 eyes, cyclosporine A 0.05% was added to the standard regimen for 12 weeks. Uncorrected visual acuity was measured 1 week and 1 and 3 months postoperatively.

RESULTS: One week postoperatively, 22 (44.9%) eyes in the cyclosporine A group and 8 (22.2%) eyes in the standard treatment group had UCVA of 20/15. Cumulatively, 36 (73.5%) eyes in the cyclosporine A group and 24 (66.7%) eyes in the standard treatment group had UCVA of 20/20 or better. One month postoperatively, 37 (75.5%) in the cyclosporine A group and 23 (63.9%) eyes in the standard treatment group had UCVA of 20/20 or better. Three months postoperatively, 40 (81.6%) eyes in the cyclosporine A group and 25 (69.4%) eyes in the standard treatment group had UCVA of 20/20 or better. Mean UCVA in the cyclosporine A group showed statistically significant improvements compared with the standard treatment group.

CONCLUSIONS: Cyclosporine A 0.05%, in the form of Restasis, may be an effective treatment for reducing the time needed for visual recovery after LASIK. Use of cyclosporine A was associated with overall better and faster recovery of UCVA. [*J Refract Surg*. 2008;24:473-476.]

Laser in situ keratomileusis (LASIK) is one of the most commonly performed ocular surgeries. Although the procedure is considered to be safe and provides the majority of patients with satisfactory outcomes, it is not without side effects. The most common adverse effect following LASIK is compromised tear production and dry eye, often lasting for 1 to 6 months following surgery.[1,2] Recent studies have indicated the status of the ocular surface and tear film before LASIK can impact surgical outcomes in terms of potential intraoperative and postoperative complications, refractive status, optical quality, patient satisfaction, and the severity and duration of dry eye after LASIK. Moreover, management of the tear film and ocular surface after LASIK can reduce the severity and duration of dry eye signs and symptoms.[2,3]

Topical cyclosporine A 0.05% (Restasis; Allergan, Irvine, Calif) has been shown to increase tear production and improve the quality of naturally produced tears. In a multicenter randomized trial, Bertelmann and Pleyer[4] reported significant improvement in the signs and symptoms of dry eye in patients with significant aqueous deficiency and keratoconjunctivitis sicca. Cyclosporine A, the active ingredient, is a cyclic polypeptide produced as a metabolite by the fungus *Tolypocladium inflatum gams*. The vehicle carrier of Restasis (Endura; Allergan) consists of glycerin, castor oil, polysorbate 80, carbomer 1342, purified water, and sodium hydroxide.

Cyclosporine A is an anti-inflammatory and immunomodulatory agent, with the ability to inhibit T-cell–mediated inflammation. In patients who suffer from dry eye, cyclo-

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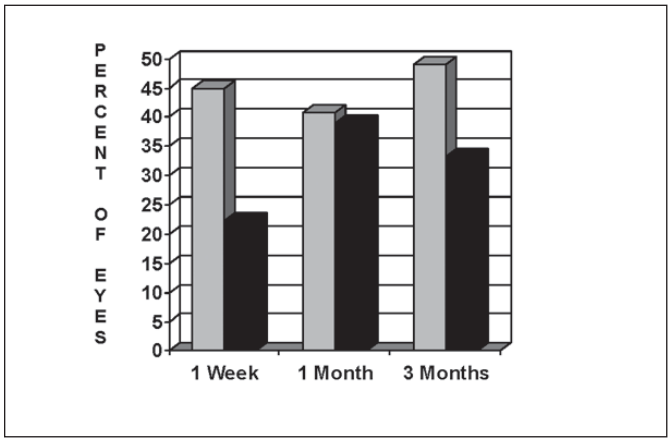

Figure 1. Percentage of eyes achieving 20/15 or better. Cumulative UCVA at 1 week and 1 and 3 months after LASIK for eyes in the cyclosporine A (gray bars) and the standard treatment (black bars) groups.

sporine A normalizes the effects of chronic dry eye disease processes of T cells and lacrimal gland acinar cells.[5] However, few studies have been published evaluating the efficacy of topical cyclosporine A on visual outcomes in LASIK patients. In one study, Salib et al[6] examined cyclosporine A use in dry eye patients undergoing LASIK and found cyclosporine A to be effective in predicting refractive results.

This study compared recovery of uncorrected visual acuity (UCVA) following LASIK in patients treated with cyclosporine A 0.05% in addition to the usual topical steroid drops, antibiotic drops, and artificial tears to patients who received a standard postoperative regimen without cyclosporine A 0.05%.

PATIENTS AND METHODS

This retrospective analysis included 45 patients (85 eyes) who underwent custom LASIK for refractive error correction (myopia or myopia with astigmatism; range: 0 to 6.00 diopters) from April 2004 through December 2004. Patients were divided into two groups: those who received a standard postoperative eye drop regimen and those who received cyclosporine A in addition to a standard postoperative eye drop regimen. This retrospective analysis was approved by the Human Research Protection Program of the University of California San Diego.

Prior to LASIK, patients underwent an ophthalmic examination that included ruling out preexisting dry eye. In all patients, preoperative evaluations included UCVA, manifest refraction, best spectacle-corrected visual acuity, cycloplegic refraction, slit-lamp microscopy, dilated fundus examination, tear breakup time, Schirmer's test, sodium fluorescein and rose Bengal staining, topography, pachymetry, and wavefront scanning.

Laser in situ keratomileusis procedures were performed by one surgeon (D.J.S.) using a VISX S4 excimer laser with CustomVue software (VISX, Santa Clara, Calif). All flaps were created using the IntraLase femtosecond laser (IntraLase Corp, Irvine, Calif). All patients received a standard postoperative treatment regimen that consisted of gatifloxacin ophthalmic solution 0.3% (Zymar, Allergan) for 7 days, prednisolone acetate 1% (Pred Forte, Allergan) for 7 days, and artificial tears (Refresh Tears; Allergan) twice daily for 90 days. Patients who were prescribed topical cyclosporine A 0.05% were instructed to use it twice daily for 90 days in addition to the standard postoperative treatment regimen. Topical cyclosporine A 0.05% is approved by the US Food and Drug Administration.

Statistical analysis was performed with SASI software (SAS Institute, Cary, NC) to calculate the basic descriptive statistics and mean UCVA in both groups.

RESULTS

Thirty-six eyes (20 patients) received a standard postoperative eye drop regimen, and 49 eyes (25 patients) received cyclosporine A 0.05% in addition to the standard regimen. In the cyclosporine A group, 35 (71.4%) eyes were in women, and in the standard treatment group, 27 (75%) eyes were in women. Mean patient age was 39.00±8.65 years (range: 26 to 59 years) in the cyclosporine A group and 39.17±9.74 years (range: 23 to 69 years) in the standard treatment group.

At 1 week postoperatively, 44.9% of eyes (22/49) in the cyclosporine A group had UCVA of 20/15 or better compared to 22.2% of eyes (8/36) in the standard treatment group. In the cyclosporine A group, 73.5% of eyes (36/49) had UCVA of 20/20 compared with 66.7% of eyes (24/36) in the standard treatment group. All (100%) of eyes in the cyclosporine A group had UCVA of 20/40 or better (20/30 or better) compared with 94.4% of eyes (34/36) in the standard treatment group. Two eyes in the standard treatment group had UCVA worse than 20/40 (20/50) (Fig 1). At the end of 1 week, a statistically significant difference was seen between the cyclosporine A and standard treatment groups even when the number of patients attaining better than 20/15 vision was considered a criteria for improvement (chi-square test).

At 1 month, 40.8% of eyes (20/49) in the cyclosporine A group had UCVA of 20/15 compared with 38.9% of eyes (14/36) in the standard treatment group. In the cyclosporine A group, 75.5% of eyes (37/49) had UCVA of 20/20 or better compared with 63.9% of eyes (23/36) in the standard treatment group. As with the 1-week data, all (100%) eyes in the cyclosporine A group had UCVA of 20/40 or better compared with 94.4% of

eyes (34/36) in the standard treatment group. Two eyes in the standard treatment group had UCVA worse than 20/40 (20/50).

At 3 months postoperatively, 49% of eyes (24/49) in the cyclosporine A group had UCVA of 20/15 compared to 33.3% of eyes (12/36) in the standard treatment group. In the cyclosporine A group, 81.6% of eyes (40/49) had UCVA of 20/20 or better compared with 69.4% of eyes (25/36) in the standard treatment group. In both groups, all eyes had UCVA of at least 20/40 or better (20/30 or better in the cyclosporine A group and 20/40 or better in the standard treatment group).

At 1 week and 3 months postoperatively, the mean UCVA of the cyclosporine A treatment group showed statistically significant improvement compared with the standard treatment group (Fig 2). Although the mean UCVA in both groups continued to improve up to 3 months, the difference between the cyclosporine A and standard treatment groups was significant ($P<.05$, Welch test).

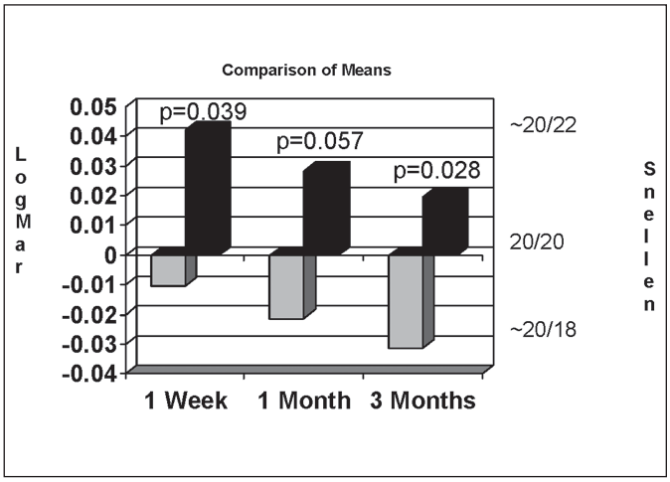

Figure 2. Mean UCVA recovery following LASIK surgery for eyes in the cyclosporine A (gray bars) and the standard treatment (black bars) groups at 1 week and 1 and 3 months postoperatively. *P* values indicate statistical significance between the two groups at all postoperative time points.

DISCUSSION

In our study, the addition of topical cyclosporine A 0.05% to the standard postoperative regimen of topical steroid and antibiotic eye drops provided a statistically significant improvement in UCVA. Overall, eyes in the cyclosporine A group showed dramatic improvement in UCVA recovery 1 week postoperatively, with 44.9% of cyclosporine A eyes obtaining UCVA of 20/15 compared with 22.2% of eyes in the standard treatment group. Cumulatively, 73.5% of eyes in the cyclosporine A group had UCVA of 20/20 or better compared with 66.7% of eyes in the standard treatment group. Furthermore, eyes in the cyclosporine A group had a mean Snellen UCVA better than 20/20 at all postoperative times examined (approximately 20/19 to 20/18 at 1 week, 1 month, and 3 months), whereas eyes in the standard treatment group had UCVA worse than 20/20 (range: 20/21 to 20/23) (Fig 2). Although the exact mechanism is not clearly understood, our results show cyclosporine A treatment following LASIK surgery was beneficial in obtaining desired visual outcome more quickly than a standard postoperative regimen.

A recent study by DiPascuale et al[7] reported dry eye after LASIK is attributed in part to delayed tear clearance, undercorrected aqueous tear deficiency, and non-recognized lipid tear deficiency. Until recently, attempts to develop therapeutic treatments for dry eye were hampered by a limited understanding of underlying pathophysiology. Although the exact mechanisms have yet to be fully defined, the current medical evidence suggests dry eye disease is the result of an underlying cytokine and receptor-mediated inflammatory process affecting both the lacrimal gland and the ocular surface.[5,8-13] Furthermore, Stern et al[14] reported most dry eye symptoms result from an abnormal, nonlubricative ocular surface that increases shear forces under the eyelid and diminishes the ability of the ocular surface to respond to environmental challenges. In the healthy eye, components of the ocular surface (ie, cornea, conjunctiva, accessory lacrimal glands, and meibomian glands), the main lacrimal gland, and interconnecting innervation act as a functional unit. When one component is compromised, normal lacrimal support of the ocular surface is impaired.

Although topical cyclosporine A 0.05% often is believed to work only after several months of treatment,[5] our study found significant differences between the eyes in the cyclosporine A and the standard treatment groups after 1 week. Similarly, a recent study by Herrygers and Noecker[15] also reported an observed treatment effect with topical cyclosporine A after 1 to 2 weeks of treatment. We believe that following LASIK, topical cyclosporine A, an immunomodulator with anti-inflammatory effects, most likely works directly on postoperative corneal inflammation.

There are several limitations to the design of this study. First, this is an open-label retrospective evaluation, with all of the shortcomings inherent to this type of design. In addition, patients who did not receive topical cyclosporine A were not given the vehicle carrier (Endura). Instead, control patients were given an artificial tear. Although we doubt that the vehicle carrier (Endura, at a twice-daily dose) would cause a significant effect on vision, future studies should include a separate group treated with this vehicle.

Our findings suggest cyclosporine A may be effective in reducing the time needed for visual recovery after LASIK surgery. However, prospective, controlled clinical studies are required to adequately determine the long-term efficacy of cyclosporine in optimizing UCVA in patients following LASIK.

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