

data collection from a large patient cohort, perhaps with collaboration from several centers, would be necessary.

JERRY A. SHIELDS, MD  
 HAKAN DEMIRCI, MD  
 BRIAN P. MARR, MD  
 RALPH C. EAGLE, JR, MD  
 CAROL L. SHIELDS, MD  
*Philadelphia, Pennsylvania*

**Reference**

1. Shields JA, Demirci H, Marr BP, et al. Sebaceous carcinoma of the ocular region: a review. *Surv Ophthalmol* 2005; 50:103–22.



**Apraclonidine and LASIK**

Dear Editor:

LASIK is a popular and relatively safe surgical procedure for the correction of myopia, hyperopia, and astigmatism.<sup>1</sup> The proper adhesion between flap and stromal bed is mandatory to restore the corneal integrity and set the background for an adequate refractive outcome properly.<sup>2</sup> Many refractive surgeons started using topical vasoconstrictors to reduce postoperative hyperemia and subconjunctival hemorrhages.<sup>2,3</sup> However, any positive effect of topical vasoconstrictors on subconjunctival hemorrhage would be rightfully overshadowed by any flap adherence problems, such as flap slippage. Although we greatly enjoyed a study conducted by Walter and Gilbert,<sup>4</sup> we were alarmed by its conclusions that the use of a vasoconstrictor, brimonidine, might increase the incidence of such complications.

Moreover, we see several flaws in the report. Apart from its not being a prospective, randomized, double-blind clinical study, the sample size seemed inadequate. A total number of 279 eyes was divided into 3 groups: the first and the last group represented the patients who underwent a standard LASIK procedure (2 control groups), whereas only the 39 eyes in between (both eyes of all patients) actually received brimonidine. Based on our understanding of flap complications, whose incidence is reported to be <2%,<sup>2,3</sup> this number of eyes represents an inadequate sample size. Moreover, the 3 groups of patients are not statistically comparable in terms of preoperative spherical equivalent (SE), gender, and age.

To overcome these problems, we conducted a prospective, randomized, double-masked study to detect the potential influence of the topical use of apraclonidine just before the LASIK procedure on postoperative flap adherence and to

see if it prevents subconjunctival hemorrhage or conjunctival hyperemia.

Sixty-six consecutive patients (32 male, 34 female) who underwent primary bilateral LASIK were included in this study. The mean age was 33±11 years (range, 18–62), whereas the mean SE was -6.43±2.03 diopters (range, -2.375 to -10.625).

Topical apraclonidine 0.125% was randomly applied only to one eye 1 hour before and 30 seconds just before placement of the vacuum ring of the microkeratome Moria M2 (Moria Surgical, Antony, France), whereas the other eye served as control (1 drop of natural tears). After laser ablation with the Allegretto Wave excimer laser (Wave-Light Laser Technology, Erlangen, Germany), the flap was floated back into position with minimal irrigation of balanced salt solution (Alcon, Fort Worth, TX) by a single surgeon (IMA).

Thirty minutes later, all the patients were examined by an independent observer (NST) to identify flap-related complications (slippage, dislocation, or flap folds) and evaluate hyperemia and subconjunctival hemorrhage.

None of the eyes from either group had any flap complications in the postoperative course, including flap adherence problems. All eyes in the apraclonidine group had a slight upper eyelid retraction, which was not present the following day. Eyes had less hyperemia and less subconjunctival hemorrhage in the apraclonidine group than in the control group ( $\chi^2$ ,  $P<0.001$ ), as shown in Table 1 (available at <http://aaojournal.org>).

Norden<sup>5</sup> conducted a double-masked study and concluded that  $\alpha$ -agonists applied topically may decrease hyperemia and subconjunctival hemorrhage after LASIK surgery significantly, without increasing the risk of flap slippage.

There are several hypotheses for possible flap adhesion problems. An explanation, considering its pharmacological mechanism of action, could be that there was a desiccation or ischemic effect on the anterior segment due to anterior ocular vessel constriction. Another possibility is a direct toxic effect on the endothelial cells,<sup>5</sup> impairing the normal functioning of the endothelial water pump and increasing the hydration of the stroma for a prolonged time, which would influence negatively the flap adherence.

However, considering the fact that there was not a proper control group in which a placebo drop would have been applied, we are led to suspect that a direct lubricant impact of the additional drop of brimonidine was not properly considered during the surgical procedure. Thus, we tend to agree with Norden<sup>5</sup> that a simpler reason, like excess of moisture on the bed and insufficient flap stroking, may be

Table 1. Postoperative Hyperemia and Subconjunctival Hemorrhage with the Topical Use of Apraclonidine in 132 LASIK Eyes

	Hyperemia				Subconjunctival Hemorrhage			
	None	Mild	Moderate	Severe	0	1	2	3
Hyperemia								
Apraclonidine	48	16	2	0	44	19	2	1
Control	7	37	22	1	19	13	20	14
				$P<0.001$				$P<0.001$

responsible for the poor flap adherence described before by Walter and Gilbert.<sup>4</sup>

In conclusion, topical apraclonidine before LASIK surgery may prevent early postoperative hyperemia and subconjunctival hemorrhage, without adverse effects on the flap adherence.

IOANNIS M. ASLANIDES, MD, PhD  
NIKOLAOS S. TSIKLIS, MD  
IOANNIS G. PALLIKARIS, MD, PhD  
MIRKO R. JANKOV, MD  
*Crete, Greece*

EFEKAN COSKUNSEVEN, MD  
EFEKAN OZKILIC, MD  
*Istanbul, Turkey*

## References

1. Pallikaris IG, Papatzanaki ME, Stathi EZ, et al. Laser in situ keratomileusis. *Lasers Surg Med* 1990;10:463–8.
2. Gimbel HV, Anderson Penno EE, van Westenbrugge JA, et al. Incidence and management of intraoperative and early postoperative complications in 1000 consecutive laser in situ keratomileusis cases. *Ophthalmology* 1998;105:1839–47, discussion 1847–8.
3. Dada T, Sharma N, Vajpayee RB, Dada VK. Subconjunctival hemorrhages after LASIK. *Laser in situ keratomileusis. J Cataract Refract Surg* 2000;26:1570–1.
4. Walter KA, Gilbert DD. The adverse effect of perioperative brimonidine tartrate 0.2% on flap adherence and enhancement rates in laser in situ keratomileusis patients. *Ophthalmology* 2001;108:1434–8.
5. Norden RA. Effect of prophylactic brimonidine on bleeding complications and flap adherence after laser in situ keratomileusis. *J Refract Surg* 2003;18:468–71.

## Author reply

Dear Editor:

I read with great interest the response to our article regarding apraclonidine and LASIK. First of all, it is quite ironic that the first criticism of our retrospective study was that it was not randomized or a masked study, when these authors are presenting their data as a letter to the editor. Indeed, our study was neither randomized nor masked, nor was it ever meant to be. It was simply an observation of our clinical findings over time—thus, a retrospective review. I did not feel it to be ethical to submit patients to a randomized trial of brimonidine, having gained the necessary knowledge from this clinical experience, nor did our institutional review board. Another criticism of our study was the small sample size of the patients having brimonidine before LASIK. Indeed, if you refer to our article, the flap slippage rate was 6 of 39 eyes, or 15%, in the brimonidine group, versus 0 of 240 eyes in the nonbrimonidine groups. Using the Fisher exact test on these 2 groups, the *P* value was highly significant at 0.00001. This powerful statistical tool tells us that there was a more than adequate sample size. Additionally, there were 2 nonbrimonidine groups, one before brimonidine use and one after. Our technique for flap reposition never changed during this entire time, so an “excess of moisture on the bed and insufficient flap stroking” do not explain

this increase in flap dislocation. The one and only variable was pretreatment with brimonidine before LASIK.

This letter to the editor is disconcerting in the lack of scientific evidence to support its conclusions. Foremost, they too had a small sample size and, by their quoted rate of 2% slipped flaps, should have found 2 or 3 slipped flaps in 132 eyes studied. One reason that slipped flaps were not seen in this study might have been the extremely short observation time (30 minutes) after the procedure. Their report does not indicate that additional observations were made on the following day. In our study, all flaps were adherent in both groups 30 minutes after surgery but were dislocated in 6 eyes on the following day. Another explanation for not observing any dislocated flaps in the apraclonidine group could be the use of the drug 1 hour before surgery. All of our patients received the drug within 5 minutes of surgery. Additionally, the authors used a very weak formulation of apraclonidine—0.125%, versus 0.5% or 1%.

However, the most likely explanation is that apraclonidine and brimonidine are 2 different  $\alpha$ -agonists, with different potency and adverse effects.

KEITH A. WALTER, MD  
*Winston-Salem, North Carolina*

## IOP after Triamcinolone Acetonide

Dear Editor:

In Jonas et al's article,<sup>1</sup> the authors discuss the treatment of raised intraocular pressure (IOP) after intravitreal injection of triamcinolone acetonide (TA). They treated 3 patients who developed intractable IOP elevation despite maximal medical treatment with filtering surgery (trabeculectomy). We offer our experience and opinions about the treatment.

Currently, there are 3 options if full medication is still unsuccessful in controlling IOP after TA injection: filtering surgery, valve implant, or vitrectomy. Steroid-induced glaucoma has been known for a long time and is due mainly to decreased outflow of aqueous. Either filtering surgery or a valve implant can increase the outflow to reduce the IOP. However, we believe it is better to find and treat the cause of elevated IOP rather than to treat the effect or complication. Therefore, the removal of vitreous TA by vitrectomy may be a better option in these cases. In addition, the occasional finding of a pseudohypopyon in the anterior chamber (AC) makes us realize that intravitreal TA can migrate to the AC and may clog the trabecular meshwork.<sup>2,3</sup> Therefore, in our clinic we performed pars plana vitrectomy (PPV) and AC irrigation to treat patients with intractable glaucoma, and IOP was well controlled rapidly after surgery.

Finally, it is of course important to control elevated IOP to avoid further optic nerve damage after intravitreal injection of TA. The choice of filtering surgery, valve implant, or vitrectomy depends on which operation the local ophthalmologist is familiar with. As retina specialists, we recommend PPV and AC irrigation.

JANE-MING LIN, MD  
YI-YU TSAI, MD  
POR-TYING HUNG, MD  
*Taichung, Taiwan*