

Changes in the Intraocular Pressure of Fellow Untreated Eyes Following Uncomplicated Trabeculectomy

Efstathios T. Detorakis, MD, PhD; Nikolaos Tsiklis, MD, PhD; Ioannis G. Pallikaris, MD, PhD; Miltiadis K. Tsilimbaris, MD, PhD

■ **BACKGROUND AND OBJECTIVE:** Previous studies have reported changes in the intraocular pressure (IOP) of fellow eyes following unilateral trabeculectomy or selective laser trabeculoplasty. This study evaluates changes in the IOP of fellow eyes following unilateral trabeculectomy and examines correlations of findings with clinical information.

■ **PATIENTS AND METHODS:** Sixty-one patients who underwent unilateral uncomplicated trabeculectomy were included. The IOP of both eyes was recorded on postoperative days 2, 3, 4, 15, 30, 60, and 90. Differences between preoperative and postoperative IOP in both eyes and correlations with clinical parameters were examined.

■ **RESULTS:** The IOP of the fellow eyes was significantly reduced on the fourth postoperative day. This reduction was significantly correlated (inversely) with central corneal thickness of fellow eyes and with the level of IOP reduction to the operated eyes.

■ **CONCLUSION:** The IOP of the fellow eyes remains largely unchanged during the first 3 months following trabeculectomy. However, a significant short-term reduction is noted on the fourth day, implying that unknown (possibly neurocrine) mechanisms may participate in the regulation of the IOP of fellow eyes.

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INTRODUCTION

Previous reports have mentioned changes in the intraocular pressure (IOP) of untreated fellow eyes

following unilateral aqueous filtering procedures.¹⁻³ Furthermore, previous studies on the unilateral application of selective laser trabeculoplasty to eyes with open-angle glaucoma have reported a significant and

From the Department of Ophthalmology, University Hospital of Heraklion, Crete, Greece.

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Address correspondence to Efstathios T. Detorakis, MD, PhD, Department of Ophthalmology, University Hospital of Heraklion, 71110, Heraklion, Crete, Greece. E-mail: detorakis@hotmail.com

sustained decrease in the IOP for the untreated fellow eyes.⁴⁻⁶ Although such responses may be difficult to explain, the possibility of a consensual ophthalmotonic response in the form of a reflex central nervous system reaction affecting the innervation of the ciliary body has been raised.¹⁻³ Moreover, in the case of changes following selective laser trabeculoplasty, a systemic release of humoral agents from the treated eye, which could then affect the IOP of the fellow eye, has been suggested.^{7,8}

The physiology of IOP control and the pathophysiology of open-angle glaucoma are still incompletely understood and probably include neuronal (neurocrine), hormonal (endocrine), and cellular (cytokine) regulation.⁹ So far, reports concerning IOP changes to the fellow eyes following unilateral trabeculectomy have been controversial because different studies have mentioned both an increase^{1,2} and a decrease³ of the mean IOP to the fellow unoperated eyes. Such disparities may be due to different inclusion criteria or surgical techniques applied and different postoperative intervals examined.

This study aims to examine the IOP in the fellow eyes following uncomplicated unilateral trabeculectomy to eyes with open-angle glaucoma in patients operated on by the same surgeon and with the same technique and evaluates correlation of findings with clinical information. Results could help in understanding the physiological mechanisms underlying IOP control following trabeculectomy and in offering guidelines for the clinical management of bilateral glaucoma cases.

PATIENTS AND METHODS

This is a retrospective consecutive case series of all patients with open-angle glaucoma in both eyes who underwent unilateral uncomplicated trabeculectomy at the Department of Ophthalmology of the University Hospital of Heraklion, in Crete, Greece. Patients who underwent surgery between 2006 and 2009 were included. Uniocular patients were excluded. All patients signed a written informed consent form in accordance with the tenets of the Declaration of Helsinki.

All procedures had been performed by the same surgeon (ETD) with the same technique under topical anesthesia, which included proparacaine eye drops and the injection of 2 mL of ropivacaine subconjunctivally. The latter was used to both anesthetize the area of flap

creation (which in primary cases was always at the 12-o'clock position of the corneoscleral limbus) and hydrodissect the conjunctiva from the underlying Tenon's capsule.

A radial conjunctival incision was performed in all cases to facilitate exposure of the scleral bed, followed by an incision along the corneoscleral limbus to create a fornix-based conjunctival flap. Wide subconjunctival dissection was then performed followed by removal of any remaining Tenon's capsule overlying the area of scleral flap. A 4 × 4 mm partial-thickness scleral flap was then marked (using monopolar diathermy) and created (using a 15° angled blade and a beaver blade) until the plane of dissection reached clear cornea (anteriorly to the scleral spur). At this point, a side port was created and then the anterior chamber was entered with a 15° blade anteriorly to the scleral spur. Trabeculectomy and iridectomy were performed (using a 0.75-mm corneoscleral punch and Vannas scissors, respectively) and the scleral flap was closed with two nylon sutures (10-0). The patency of trabeculectomy was tested by injecting balanced salt solution from the side port and observing the outflow from the trabeculectomy site. At that point, adjustment of suture tying was performed as needed.

The conjunctiva was then closed with two tight polyglactin 910 sutures (7-0) at the ends of the fornix-based flap, forcing the conjunctiva firmly against the scleral bed to effectively seal the wound along the limbus. The remaining radial incision was also sutured with 7-0 polyglactin 910 sutures. In case a secondary trabeculectomy was performed following failed primary procedures (ie, for patients who necessitated oral acetazolamide to control the IOP), the procedure was repeated in the same way, always nasally to the initial site (at the superior-nasal conjunctiva) to preserve the superior-temporal quadrant for possible future anti-glaucomatous valve implantation. Mitomycin C 0.2% was also used (applied episclerally for 2 min) in selected cases, according to previously proposed protocols.¹⁰

According to the practice followed in our department, all topical medications and oral acetazolamide were discontinued to the operated eye immediately after trabeculectomy. Instead, topical medications were continued unchanged in the fellow eyes. Furthermore, all patients were discharged on the fourth postoperative day and were examined at regular postoperative intervals, again according to the standard practice of our

TABLE 1
Mean IOP Values (mm Hg) at All Intervals in Both Operated and Fellow Eyes

Interval	IOP (OE)	<i>P</i> ^a	IOP (FE)	<i>P</i> ^a
Preoperative	24.45		17.15	
2nd day	11.36	.00	17.09	.49
3rd day	11.01	.00	17.12	.33
4th day	10.77	.00	15.84	.04
15th day	16.19	.00	18.36	.06
30th day	16.96	.01	17.09	.62
60th day	16.42	.01	18.15	.06
90th day	15.53	.00	16.30	.08

IOP = intraocular pressure; OE = operated eyes; FE = fellow eyes.

^a*Statistical significance of differences between preoperative and postoperative intervals (paired samples *t* test).*

department. Based on this follow-up schedule, the IOP (by Goldmann applanation tonometry) was recorded from patients' charts in both eyes on postoperative days 2, 3, 4, 15, 30, 60, and 90. All IOP measurements took place in the morning (10.00 ± 1 hr), in accordance with the prior data on the peak IOP in the Greek population.¹¹ In all cases, the central corneal thickness, the status of the lens (phakic, aphakic, or anterior of posterior chamber lens implant), and the age and gender were also recorded from patients' charts.

Overall, 61 patients aged 70.49 ± 9.90 years (range: 36 to 88 years) were included (38 men, 62.29%). Central corneal thickness was 517.87 ± 35.36 μm (range: 436 to 619 μm) for the operated eyes and 519.24 ± 52.93 μm (range: 439 to 714 μm) for the fellow eyes. ALAQ1 was 23.29 ± 1.17 mm (range: 21.40 to 28.64 mm) for the operated eyes and 23.30 ± 1.13 mm (range: 21.27 to 28.33 mm) for the fellow eyes. At each interval, the difference between the preoperative and postoperative IOP (dIOP) was calculated for both operated eyes and fellow eyes.

Statistical analysis was performed using SPSS 8.0 software (SPSS, Chicago, IL). Statistical significance was set at a *P* value of .05. The two-tailed paired-samples *t* test was performed for the comparison of preoperative and postoperative IOP values for both fellow eyes and operated eyes. Pearson's bivariate correlation coefficient was used for the evaluation of correlations between dIOP and central corneal thickness, ALAQ1, or age (on all postoperative intervals), for both operated eyes and fellow eyes. Furthermore, Pearson's bivariate correlation coefficient was used for the evalua-

tion of correlations between the IOP and dIOP of the operated eyes and that of the fellow eyes on all intervals. Differences in dIOP associated with the phakic status of the fellow eyes or with the intraoperative use of mitomycin C were examined with one-way analysis of variance (ANOVA).

RESULTS

The IOP of the operated eyes was significantly reduced on all postoperative intervals compared with preoperative values (paired samples *t* test). On the contrary, the postoperative IOP of the fellow eyes did not significantly differ from respective preoperative IOP levels on all intervals except for the fourth day (on which it was significantly reduced). IOP values of all intervals for both operated eyes and fellow eyes and the statistical significance of respective differences are presented in Table 1, whereas dIOP scores and the percentage of IOP reduction in both operated eyes and fellow eyes are presented in Table 2. The IOP scores at all intervals (preoperative and postoperative) for both operated eyes and fellow eyes are presented in Figure 1. The dIOP scores at all intervals (preoperative and postoperative) for both operated eyes and fellow eyes are presented in Figure 2.

On the fourth postoperative day, the dIOP in the fellow eyes was significantly correlated (inversely) with central corneal thickness of the fellow eyes (Pearson bivariate correlation coefficient -0.42, *P* = .02) and with the preoperative levels of IOP for both operated eyes (Pearson bivariate correlation coefficient 0.30, *P*

TABLE 2
dIOP Scores and Percentage of IOP Reduction in Operated Eyes and Fellow Eyes at the Intervals Examined

Interval	dIOP OE (mm Hg)	IOP Reduction in OE (%)	dIOP FE (mm Hg)	IOP Reduction in FE (%)
2nd day	13.09	53.54	0.06	0.35
3rd day	13.44	54.97	0.03	0.17
4th day	13.68	55.95	1.31	7.64
15th day	8.26	33.78	-1.21	-7.06
30th day	7.49	30.63	0.06	0.35
60th day	8.03	32.84	-1	-5.83
90th day	8.92	36.48	0.85	4.96

dIOP = difference in preoperative and postoperative intraocular pressure; IOP = intraocular pressure; OE = operated eyes; FE = fellow eyes.

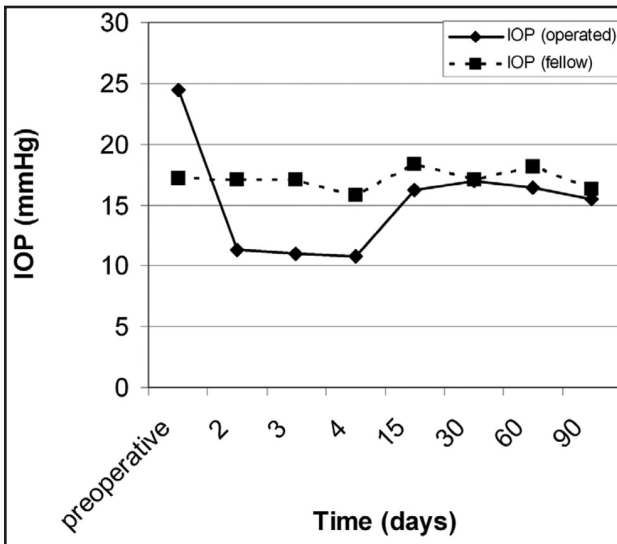


Figure 1. Intraocular pressure (IOP) scores (mm Hg) at all intervals (preoperative and postoperative) for both operated eyes and fellow eyes.

= .04) and fellow eyes (Pearson bivariate correlation coefficient 0.32, $P = .03$). Furthermore, the dIOP of the fellow eyes on the fourth postoperative day was significantly correlated with dIOP of the operated eyes on the same interval (Pearson bivariate correlation coefficient 0.42, $P = .40$). The correlations of dIOP on the fourth postoperative day with patient's age were statistically not significant. On the fourth postoperative day, the difference in dIOP between males and females, as well as the variation of dIOP of the fellow eyes according to the phakic status of fellow eyes, were also statistically not significant (Pearson's chi-square test and one-way ANOVA, respectively). On the contrary, the

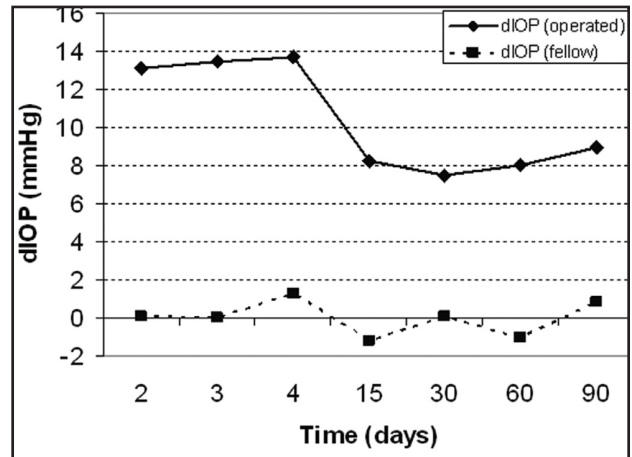


Figure 2. Difference in intraocular pressure (dIOP) scores (mm Hg) at all intervals (preoperative and postoperative) for both operated eyes and fellow eyes.

dIOP score of both the operated eyes and fellow eyes was significantly higher for cases receiving mitomycin C compared with unenhanced cases (ANOVA F value 2.98, $P = .02$ and ANOVA F value 2.53, $P = .04$, respectively).

DISCUSSION

This study evaluated IOP changes in the fellow eyes following trabeculectomy for the management of medically uncontrolled open-angle glaucoma. Results imply that the IOP of the fellow eyes is largely unchanged on most intervals during the first 3 months following trabeculectomy, except for the fourth postoperative day. On that interval, the IOP of the fellow eyes is significantly reduced compared with preopera-

tive levels, and this reduction is associated with central corneal thickness of the fellow eyes and the preoperative IOP levels for both operated eyes and fellow eyes.

A previous study concerning the effects of trabeculectomy on the aqueous humor flow of the unoperated fellow eyes of patients with bilateral primary open-angle glaucoma also reported that the typical changes in IOP observed in the unoperated eyes may be noted on the third and fourth day after unilateral filtration surgery.¹ However, that study detected an increase in aqueous flow (and a consequent increase, rather than decrease, in IOP) for the unoperated eyes, possibly representing a compensatory effort triggered by the reduced anterior chamber volume of the operated eyes.¹ This consensual reaction was attributed to changes in central nervous system regulation of ciliary body innervation.¹ A study by Yarangümelı et al. also found an increase in IOP for untreated eyes following unilateral trabeculectomy during a 3-month follow-up.² On the contrary, a more recent study by Vysniauskiene et al. detected a decrease in IOP of untreated fellow eyes following trabeculectomy, implying that the regulatory mechanisms affecting IOP changes of the untreated fellow eyes may be more complex.³ Findings from the current study are in agreement with the latter report. Taking into account that IOP changes in fellow eyes have been largely attributed to altered aqueous production, instead of altered aqueous outflow, such findings imply that a suppression, rather than induction, of ciliary body activity of the fellow eyes may predominate in the first few postoperative days.

A recent study on IOP changes in the fellow untreated eyes following selective laser trabeculectomy has reported that although the IOP decrease in the untreated eyes was not apparent until 2 weeks following treatment, it was, nonetheless, comparable to that for the treated eyes in both size (1.2 to 4.7 mm Hg, corresponding to 4.9% to 28.6% of the pretreatment IOP) and duration (for the intervals between 2 weeks and 6 months following selective laser trabeculectomy).⁴ In the current study, IOP changes in the fellow eyes were much less pronounced on most intervals examined, compared with similar reports on selective laser trabeculectomy. Furthermore, the time pattern of IOP changes in the fellow eyes was considerably different than that in selective laser trabeculectomy because changes were more pronounced in the immediate post-trabeculectomy interval (peaking on the fourth postoperative day).

This finding possibly implies that the pathophysiological mechanisms dominating such changes are also different. In the case of selective laser trabeculectomy, humoral agents such as interleukin-1a, interleukin-1b, and tumor necrosis factor- α or matrix metalloproteinases are possibly released as a result of tissue–laser interaction in the treated eyes and are then dispersed systemically to affect the fellow eye.^{12,13} In the case of trabeculectomy, tissue–laser interactions are, of course, absent but a sharp reduction in IOP takes place on the immediate postoperative intervals. The collapse of IOP at the operated eyes might act as a stimulus (potentially by triggering neural signals affecting aqueous production) in both eyes. The possibility that the neuronal input to the ciliary body may be affected by peripheral signals has also been previously proposed.⁹

Alternatively, the IOP at the fellow eyes may be affected by blood flow changes at the operated eyes. Hemodynamic changes in the ocular (especially uveal) circulation have been described following trabeculectomy, associated with the sharp drop in IOP during the first postoperative days.^{14,15} Such changes may trigger feedback regulatory vascular changes affecting uveal circulation in both eyes. Both aqueous production and aqueous outflow (especially through the uveoscleral pathway) could potentially be affected by such changes.

The fact that postoperative IOP changes of the fellow eyes were most pronounced (and statistically significant) on the fourth postoperative day possibly reflects a time interval required for the build-up of a vasogenic or neurocrine feedback response (derived from IOP changes at the operated eyes). Furthermore, the fact that the IOP was inversely correlated with the central corneal thickness of the fellow eyes may possibly reflect an increased susceptibility of eyes with a low central corneal thickness score to stimuli mediating IOP regulation. The fact that dIOP at the fellow eyes was significantly more pronounced in cases receiving mitomycin C may be attributed to the more pronounced dIOP in the operated eyes in such cases,¹⁶ which could possibly trigger a more powerful hypotensive stimulus for the fellow eyes. This could be related either to IOP-mediated neurocrine signals, as previously mentioned or, alternatively, to potential effects by mitomycin C on the ciliary body epithelium because the intraocular diffusion of mitomycin C following episcleral intraoperative application has been documented by previous studies.^{17,18}

The relatively small number of cases, the retrospective design, and the short (3-month) follow-up period may be considered weak points of this study. On the other hand, the consecutive data collection and the fact that all cases were operated on by the same surgeon and managed under the same postoperative treatment protocol possibly enhance the validity of results. Further research, probably involving clinical and experimental studies, would be required to clarify the exact mechanisms underlying IOP changes in the fellow eyes following a trabeculectomy. Results could help in improving the treatment of patients with bilateral glaucoma and in better understanding the physiology of IOP regulation.

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AUTHOR QUERIES

AQ1 Please define the abbreviation.

AQ2 Please provide pages for the chapter.