Impact of intraocular pressure after filtration surgery on visual field progression in primary open-angle glaucoma

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PURPOSE. *To compare visual field progression after trabeculectomy in eyes showing a postoperative intraocular pressure (IOP) less than or equal to 16 mmHg and eyes with an IOP of 17 to 21 mmHg.*
METHODS. *A retrospective cohort study design was used. A total of 101 eyes of 101 consecutive patients undergoing trabeculectomy for primary open-angle glaucoma (POAG) with a postoperative IOP less than or equal to 21 mmHg were divided into two groups: Group 1 included eyes showing a postoperative IOP less than or equal to 16 mmHg at all visits and Group 2 included eyes with a postoperative IOP between 17 and 21mmHg. In turn, each of these groups was divided into two subgroups according to whether treatment was required for IOP control. Glaucomatous visual field control during follow-up was compared between the subject groups.*
RESULTS. *Kaplan-Meier analysis revealed glaucomatous visual field control in 98.53% of the eyes in Group 1 and 89.06% of those in Group 2 at 5 years, the difference between the groups being significant.*
CONCLUSIONS. *Glaucomatous disease progression is less frequent when IOP is less than or equal to 16 mmHg in all the follow-up visits after trabeculectomy. The results indicate a definite benefit of low IOP in visual field control. (Eur J Ophthalmol 2007; 17: 357-62)*

KEY WORDS. *Glaucoma, Trabeculectomy, Visual field progression*

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INTRODUCTION

A relationship between high intraocular pressure (IOP) and the development of glaucoma was suspected as early as 1622, when Bannister first mentioned this link. However, it took until the 19th century to confirm the suspicion (1-5). Recent studies such as the Early Manifest Glaucoma Trial (EMGT) (6, 7) show that by decreasing IOP with hypotensive medication by 25% in patients with incipient open-angle glaucoma, the risk of visual field progression is reduced in 50% of cases. Moreover, the Ocular Hypertension Treatment Study (OHTS) concluded that topical antiglaucomatous medication is effective at preventing or delaying the appearance of primary open-angle glaucoma (POAG) in subjects with high IOP (8, 9).
IOP thus appears to be the main risk factor for the onset of glaucoma and its reduction has been associated with diminished visual field progression (10). Nevertheless, recent studies have shown that an IOP under 21 mmHg may be insufficient to prevent visual field deterioration in glaucoma (11-16). The aim of the present study was to compare visual field progression after trabeculectomy in eyes showing a postoperative IOP less than or equal to 16 mmHg and eyes with an IOP of 17 to 21 mmHg.

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MATERIALS AND METHODS

The charts of all consecutive patients who underwent a trabeculectomy between January 1996 and January 2000 were reviewed. Data were collected for one eye only of each subject in the study. If both eyes required surgery, the one with the greater IOP entered the study. The criteria for inclusion were a diagnosis of primary open-angle glaucoma, age older than 25 years, access to at least three reliable baseline preoperative visual fields, no previous glaucoma or cataract surgery, no cataract surgery during follow-up, a minimum follow-up of 2 years after surgery, postoperative IOP below 21 mmHg, and no retinal or neurologic disease that may have affected the visual field. Our group does not use intraoperative or postoperative antimetabolites. The two study groups established were Group 1, including eyes showing a postoperative IOP less than or equal to 16 mmHg at all visits, and Group 2, comprised of eyes with a postoperative IOP between 17 and 21 mmHg.

Primary open-angle glaucoma was defined as the presence of a reproducible visual field defect consistent with glaucoma and the appearance of the optic disc, along with a pretreatment IOP of 21 mmHg or more, and an open angle with no signs of secondary causes of glaucoma. A visual field defect consistent with glaucoma was defined as the presence of 1) abnormal glaucoma hemifield test, confirmed on three consecutive tests, or 2) three abnormal points confirmed on three consecutive tests, with p<5% probability of being normal, one of which should have p<1%, all being not contiguous with the blind spot, 3) CPSD <5% if the visual field is otherwise normal, confirmed on three consecutive tests. This is modified from criteria of the EGS guidelines (17, 18) that require the VF defect to be confirmed on two consecutive tests.

While the patient was under maximally tolerated medical therapy, indications for surgery were an IOP that in the examiner's opinion represented a high risk of glaucomatous progression, worsening of the visual field as judged by the examining physician, or deterioration of the optic disc as judged by the physician. All patients underwent a Watson-type trabeculectomy (19-23).

The preoperative data collected were age at the time of surgery, race, sex, history of systemic disease, use of systemic medication, previous laser trabeculoplasty, IOP, number of antiglaucoma medications used, and three reliable baseline preoperative visual fields (17, 18).

Postoperative measurements included best-corrected visual acuity, IOP, and visual field progression. Also recorded was the number of antiglaucoma medications used.

IOP was measured with the Perkins applanation tonometer (Clement Clarke International Ltd., London, UK) (24). The patient's visual field status was monitored by automated perimetry measurements (24-2 of Humphrey Field Analyzer, size III white stimulus, and full threshold strategy, Humphrey Instruments, Palo Alto, CA). Visual field loss was classified as early, moderate, or severe, according to the classification by Hodapp et al (25). Visual field deterioration was defined as follows: a reproducible 10 dB loss or greater at two or more contiguous points in Bjerrum's area, a reproducible 5 dB loss or greater at three or more contiguous points occurring in Bjerrum's area in a normal hemifield, an appearance of a 10-dB difference across the nasal horizontal midline at two or more adjacent locations, or worsening of this difference or a minimum reproducible loss of 10 dB at a minimum of three test locations (26). Definitive progression was considered if any of these findings was observed on at least three consecutive visual fields. We have in all patients two visual fields per year. If a new defect was observed, two visual fields in the next 3 weeks were made to confirm the progression.

Topical antiglaucoma medications were added when a worsening of the visual field was observed and/or IOP was not acceptable as judged by the physician.

Quantitative data are presented as the mean ± standard deviation. In each case, variable distribution was checked using theoretical models and the hypothesis of homogeneity of variance was contrasted. In each hypothesis contrast, an a or type I error of less than 0.05 of the null hypothesis was rejected. Repeated measures analysis of variance was performed using a random effect factor. The Levene test for variance similarity was performed before the Student *t*-test for before and after treatment group-wise comparisons. The Bonferroni correction was applied in multiple contrasts. Chi-square or Fisher exact text was used for qualitative data. Time-to-failure curves were constructed through Kaplan-Meier survival analysis, with significance among groups determined using the Breslow test. Statistical analysis was performed using windows SPSS version 12 software (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 101 eyes of 101 patients fulfilled the inclusion criteria. Table I shows the preoperative characteristics of our patient population. All the participants were white. Of the 101 eyes, 68 were included in Group 1 since they showed a postoperative IOP less than or equal to 16 mmHg in all visits. The remaining 33 eyes with a postoperative IOP of 17 to 21 mmHg were assigned to Group 2.

Mean follow-up was 4.75±1.59 years in Group 1 and 4.97±1.77 years in Group 2 and median follow-up was 5 years in both groups, indicating no significant differences (p=0.6). Significant differences were observed between these groups in terms of final medications, final IOP, and the percentage fall in IOP, as shown in Table I.

No statistically significant differences were observed between the groups in terms of age, sex, initial number of medications, initial visual acuity, final visual acuity, initial IOP, degree of preoperative visual field defects, and previous argon laser trabeculoplasty (Tab. I).

When we analyzed complications, 22 eyes showed postoperative hyphema (16 Group 1 and 6 Group 2 eyes) that resolved 1 to 2 weeks after conservative treatment. No major complications were encountered.

Figure 1 provides Kaplan-Meier curves of time to failure in terms of glaucomatous visual field control, and indicates percentage successes at 5 years. Results indicated that glaucomatous disease was controlled in 95.96% of the eyes in Group 1 versus 86.58% in Group 2 at 5 years. Thus, glaucomatous visual field control was significantly better (p<0.05) when postoperative IOP was less than or equal to 16 mmHg at each follow-up session.

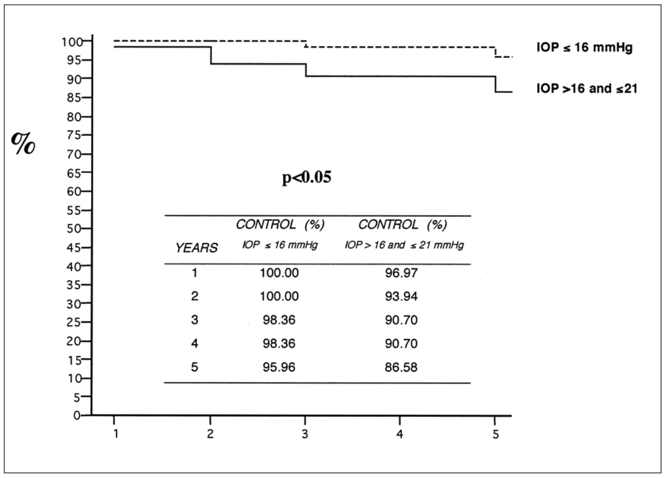

Fig. 1 - *Kaplan-Meier survival analysis. Glaucomatous disease control in eyes with postoperative intraocular pressure less than or equal to 16 mmHg in all visits (Group 1) and in eyes with a postoperative intraocular pressure between 17 and 21 mmHg (Group 2).*

Table II shows the subgroups formed according to whether medical treatment was required or not after surgery. It may be observed that 46 eyes (67.6%) did not require treatment in Group 1, versus 13 eyes (39.4%) in Group 2 (p<0.05).

TABLE I - CHARACTERISTICS OF BOTH GROUPS OF EYES

	Group 1 (n=68), IOP ≤16 mmHg (mean ± SD)	Group 2 (n=33), IOP >16 and ≤21 mmHg (mean ± SD)	p value
Age, yr (range)	65.9 ± 13.0 (32–85)	62.39 ± 13.7 (25–84)	0.17
Male, n (%)	33 (48.5)	15 (45.5)	0.77
Female, n (%)	35 (51.5)	18 (54.5)	
Initial medications	1.8 ± 0.7	1.9 ± 0.8	0.54
Final medications	0.4 ± 0.7	0.9 ± 0.8	<0.05
Initial VA (Snellen)	0.7 ± 0.2	0.7 ± 0.2	0.35
Final VA (Snellen)	0.5 ± 0.2	0.6 ± 0.2	0.70
Initial IOP (mmHg)	26.1 ± 5.3	25.3 ± 3.0	0.78
Final IOP (mmHg)	13.4 ± 2.1	18.5 ± 1.2	<0.05
Degree of IOP reduction (%)	47.04 ± 12.17	20.12 ± 9.35	<0.05
Prior ALT, n (%)	59 (86.76)	27 (81.81)	0.51
No Prior ALT, n (%)	9 (13.24)	6 (18.19)	
Initial visual field defect, n (%)			
Early	11 (16.2)	12 (36.4)	0.06
Moderate	18 (26.5)	9 (27.3)	
Severe	39 (57.4)	12 (36.4)	

IOP = Intraocular pressure; SD = Standard deviation; VA = Visual acuity; ALT = Argon laser trabeculoplasty

TABLE II - POSTOPERATIVE MEDICATION AT LAST VISIT

	Number of medications				Total
	0	1	2	3	
Number of cases with IOP >16 and ≤21 mmHg	13	11	8	1	33
Number of cases with IOP ≤16 mmHg	46	12	10	0	68
Total	59	23	18	1	101

IOP = Intraocular pressure

DISCUSSION

It is widely accepted that the randomly established controlled IOP threshold value of 21 mmHg is not the best way of measuring the success of filtration surgery (27, 28). This pressure limit has been applied since 1958, when Leydecker et al determined IOP in 10,000 subjects by indentation tonometry to give an average of 15.5±2.6 mmHg (29). Using this figure, the upper limit of normality can be calculated as two standard deviations over the mean (21 mmHg), which is why most authors applied the value of 21 mmHg as the ideal threshold for postoperative IOP (30).

We should therefore consider the extent to which the size of the pressure drop may affect the control of glaucomatous disease. Our study is based on other studies such as the Advanced Glaucoma Intervention Study (AGIS). This study supports that achieving low levels of IOP slows the progression of glaucomatous optic neuropathy (11). Other studies have observed similar evidence (12-16). Therefore, the greater the percentage reduction in IOP, the lower the risk of subsequent visual field progression (31).

The AGIS assesses IOP during follow-up without taking into account the glaucoma management employed to achieve IOP control. Their goal was to maintain IOP less than 18 mmHg (11). In contrast, in our study we decided to divide eyes with POAG into two groups according to whether their IOP after trabeculectomy was less than or equal to 16 mmHg in all visits (Group 1) or 17 to 21 mmHg (Group 2). Although many techniques are available for classifying a visual field as normal or glaucomatous, there is less agreement about the optimal method for assessing progression of visual field loss over time (32-39). In this study visual field progression was defined by criteria described by Nouri-Mahdavi et al (26).

The number of final medications was 0.4±0.7 in Group 1 and 0.9±0.8 in Group 2 ($p=0.01$). This would be expected, since patients in whom it is possible to achieve a greater IOP reduction are going to require a lower number of drugs. The final IOP of 13.4±2.1 mmHg for Group 1 and 18.5±1.2 mmHg for Group 2 ($p<0.005$) can also be easily explained by the criteria used to assign the eyes to each of the groups.

It may also be noted that eyes in Group 2 with an IOP between 17 and 21 mmHg showed an 86.58% rate of glaucomatous visual field control at 5 years compared to the Group 1 eyes with an IOP less than or equal to 16 mmHg, in which 5-year visual field control was achieved in 95.96%, the difference being statistically significant ($p<0.05$) (Fig. 1). This indicates it is not only important to reduce the IOP to below 21 mmHg, but that when the IOP is decreased to an arbitrary limit such as 16 mmHg, the control of glaucoma is significantly better.

Our findings corroborate other reports regarding the significance of a lower IOP during follow-up. In AGIS, eyes with IOP under 18 mmHg in all visits during the first 6 years of follow-up were least likely to show worsening (11). Some years ago, Werner et al reported that the prognosis for further field loss seemed to be better if postoperative IOP was controlled at lower levels and did not fluctuate widely (40). Recently, Nouri-Mahdavi et al observed that IOP fluctuation remained a significant predictor of visual field progression (41).

On the other hand, the initial test on automated perimetry may be difficult or stressful. The results improve as the subject gains more experience performing the test (42-45). A patient new to perimetry should undergo at least three test sessions, to establish a baseline for subsequent comparisons. This is the standard procedure in our hospital and for this reason we used it in our study.

Several potential limitations to this study should be noted. The retrospective nature of this study with the potential for selection bias and nonstandardized data collection are limiting factors. All of our cases were white, so these results may not be extrapolated to other populations. We studied patients operated on between 1996 and 2000, so we did not take into account the corneal pachymetry based on the results from the OHTS (46). Therefore, we know that corneal thickness appears to be a strong predictive factor for the development of POAG. Finally, the Normal Tension Glaucoma Study investigators reported that the effect of the reduction of IOP on progression of visual change in normal tension glaucoma was found only when the impact of cataract was removed (15); our study was retrospective and the effect of the cataract on the visual field was not studied.

Nevertheless, our findings suggest that the control of glaucomatous disease after trabeculectomy in POAG is better if surgery manages to achieve an IOP below 16 mmHg.

Proprietary interest: None.

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