The effect of anti-glaucomatous therapy discontinuation after successful GATT surgery on outcome and progression in open-angle glaucoma

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ABSTRACT

Purpose: To evaluate the effect of discontinuation of anti-glaucomatous therapy after GATT±phacoemulsification on outcomes and disease progression in patients with mild to moderate open-angle glaucoma

Materials and Methods: Patients who underwent GATT±phacoemulsification for primary open angle or pseudoexfoliative glaucoma and who were followed up for at least one year were divided into two groups as patients in whom anti-glaucomatous agents were continued in the postoperative period (Group 1) and anti-glaucomatous agents were discontinued (Group 2). Preoperative and postoperative ocular examination findings, mean retinal nerve fibre layer thickness (mRNFLT) by optical coherence tomography and mean deviation (MD) by standard automated perimetry were recorded. Pre/post-operative changes were analysed statistically within and between groups.

Results: Preoperative mean intraocular pressure (IOP) was 26.7±7.1 and 28.6±4.4 mmHg in groups 1 and 2, respectively (p=0.235). Central corneal thickness, iridocorneal angle and degree of pigmentation in the angle were similar between groups. The change in mean IOP at one-year follow-up was similar in both groups (p=0.087). There was no significant change in mean mRNFLT and MD for both groups in all postoperative measurements. Anti-glaucomatous medications decreased significantly in both groups at 12 months postoperatively, with significantly greater reduction in group 2 (p=0.032).

Conclusion: The findings of our study suggest that discontinuation of anti-glaucomatous agents after successful GATT ± phacoemulsification surgery has no effect on IOP change and disease progression in patients with mild-moderate open angle glaucoma. Nevertheless, it should be noted that postoperative follow-up should be performed appropriately as some cases may require reuse of anti-glaucomatous agents.

Keywords: intraocular pressure, glaucoma progression, gonioscopy assisted transluminal trabeculotomy, open angle glaucoma

INTRODUCTION

Glaucoma is estimated to affect more than 110 million people globally by 2040, making it the leading cause of irreversible blindness.[1] Glaucoma is a chronic, progressive and typically asymptomatic.[2] People with glaucoma are at a lifetime risk of progression to severe vision loss and even blindness.[2] Intraocular pressure (IOP) is the only modifiable risk factor to avoid the progression of glaucoma, and the only generally accepted treatment that has been shown to be effective in preventing the progression of glaucoma is IOP reduction.[3] Initial approach for the management of glaucoma patients is the use of medical therapy and/or laser treatment.[4,5,6] Surgical treatment is usually needed if the target IOP cannot be achieved, when the patient is not

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compliant with the treatment or when serious side effects occur due to topical anti-glaucomatous agents.[7]

Gonioscopy-assisted transluminal trabeculotomy (GATT) is a conjunctiva-sparing ab-interno minimally invasive glaucoma surgery in which the trabecular meshwork and the inner wall of Schlemm's canal are circumferentially incised to facilitate the passage of aqueous humour through the collecting ducts and episcleral veins.[8] Since its initial description, a number of studies have been conducted that demonstrate safety and efficacy of treatment in people with different types of open-angle glaucoma.[9,10,11] Sudden increases in IOP after GATT surgery are common, with an incidence of up to 37%.[12] This is particularly concerning in eyes with significant damage to the optic nerve, as increased IOP can lead to progression of glaucomatous damage, which carries significant risk in terms of rapid progression.[13]

Although there are studies on the efficacy, safety and possible complications of this surgery, there is a limited body of knowledge regarding the characteristics, temporal onset, risk factors, course, management and prognosis of sudden intraocular pressure (IOP) increases, which are observed with relatively high frequency in the postoperative period. In this study, we aimed to evaluate the effect of discontinuation of anti-glaucomatous therapy after GATT surgery on outcomes and disease progression at one-year follow-up in patients with mild to moderate open-angle glaucoma.

MATERIALS AND METHODS

The medical files of patients who underwent GATT surgery for primary open angle glaucoma (POAG) or pseudoexfoliative glaucoma (PEG) between January 2022 and December 2022 were retrospectively reviewed. The study was approved by the University Ethics Committee (Date:03.04.2024, meeting number:12) and was carried out in adherence to the ethical principles outlined in the Declaration of Helsinki. As the study was retrospective in nature, the patients were not provided with informed consent.

Individuals over the age of 18 years with mild to moderate POAG or PEG, whose IOP could not be controlled with maximally tolerated medical treatment or who showed progression despite normal IOP were included in the study. Patients with ocular diseases other than mild-moderate POAG/PEG (such as corneal leukoma, uveitis and retinal vascular diseases, etc.), a history of ocular surgery other than cataract surgery and patients without at least one year of postoperative follow-up were excluded. Patients who developed any complication during phacoemulsification were excluded from the study. The 64 eyes of 64 patients who underwent GATT or phacoemulsification + GATT surgery were divided into two groups as patients in whom preoperative anti-glaucomatous treatment was continued (Group 1) and patients in whom treatment was discontinued (Group 2). Although the patients were seen at intermediate visits, ophthalmological examination findings of the patients on preoperative and postoperative day one and at first, third, sixth months and at first year were recorded for this study. Patients who experienced any complications following surgery or as required by the physician were subject to additional evaluation at correspondingly appropriate time intervals. Mean retinal nerve fibre layer thickness (mRNFLT) obtained from optical coherence tomography (OCT) examinations (Spectralis, Heidelberg Engineering; Heidelberg, Germany), which was performed preoperatively and at first, third and sixth months and first year postoperatively, were recorded. Visual field tests, performed with standard automated perimetry (SAP) 24-2 (Humphrey Field Analyzer; Carl Zeiss Meditec, Inc., Dublin, CA, USA) preoperatively and at postoperative first year, were evaluated and mean deviation (MD) results were recorded. Best corrected visual acuity (BCVA) at each examination, biomicroscopy examination findings, gonioscopy findings with a 4-mirror goniolens (Volk G-4 Mirror Gonio Lens, Volk Optical, Inc.), IOP values with the same calibrated Goldmann applanation tonometer, fundoscopy findings and number of medications used were documented. Snellen visual acuities were converted to logMAR for statistical analysis.

All surgeries were performed by two surgeons under topical or peribulbar anaesthesia. One end of the 5-0 prolene suture was blunted with cautery before the surgery is initiated. After phacoemulsification and intracapsular IOL implantation (for patients who needed cataract surgery), the anterior chamber was formed with viscoelastic material (1% sodium hyaluronate). After the head of the patient was rotated 35-45° away from the surgeon and the operating microscope was tilted 35-45° downwards towards the surgeon to maximize visualisation of the nasal angle. Using the same viscoelastic, a surgical goniolens was placed over

the cornea to ensure full visualisation of the nasal angle and trabecular meshwork. A 25G needle was used to make goniotomy the trabecular meshwork at the nasal angle. Viscoelastic was reapplied to the goniotomy site to dilate Schlemm's canal and to remove the hemorrhage from the surgical field. The blunt 5-0 prolene suture was advanced into Schlemm's canal (to the full 360° canalisation) using 20G forceps. Using the same forceps, the tip of the suture was pulled out of the eye through a clear corneal incision. The distal end of the suture and the paracentrally inserted fragment were then gently withdrawn simultaneously to complete the trabeculotomy. If 360° progression in the canal could not be achieved, an additional paracentesis was opened and the blunt suture was advanced in the opposite direction in the Schlemm's canal to complete the trabeculotomy. Eyes in which the Schlemm's canal could be cannulated at least 180° or more were included in the study.

All patients received postoperative topical antibiotic (moxifloxacin) and steroid (dexamethasone) drops. Topical antibiotic was discontinued in the second week, while topical steroid was reduced by one drop per week for a total of 4 weeks. One of the surgeons discontinued anti-glaucomatous drops in patients with normal IOP in the postoperative period, while the other surgeon preferred to use anti-glaucomatous drops for another 15 days even if the postoperative IOP was within normal limits.

Surgical success was defined as a decrease in IOP by at least 20% compared to the preoperative period or a postoperative IOP below 22 mmHg.[14] Failure was defined as corneal decompensation or visual loss at any time during the follow-up period or the need for repeat glaucoma surgery. Patients in whom surgical success could not be achieved were not included in the study.

Statistical analysis

Statistical Package for the Social Sciences version 20 (IBM, SPSS version 20.0; IBM, New York, NY, USA) was used for statistical analysis. The distribution of quantitative data was evaluated by Kolmogorov-Smirnov test. Descriptive variables were expressed as mean ± standard deviation for normally distributed ones and median (min-max) for non-normally distributed ones. Categorical variables were expressed as number of cases and percentage. Paired t test and repeated measures analysis of variance test were used to compare data within groups, while Student t test and repeated measures two-way ANOVA test were used for comparisons between groups. In order to compare non-normally distributed data between the groups, Mann-Whitney U test was used. A chi-square analysis was employed for the purpose of comparing categorical data. The results were analysed using a 95% confidence interval. The level of significance has been set at 0.05.

RESULTS

There was no difference between group 1 (n=37) and group 2 (n=27) in terms of mean age and the distribution of gender and diagnosis (Table 1). The mean preoperative IOP was 26.7 ± 7.1 mmHg in group 1 and 28.6 ± 4.4 mmHg in group 2 (p=0.235). Other preoperative examination findings and SAP and OCT findings of the eyes included in the study are also summarised in Table 1. There was no

Table 1: *A comprehensive comparison of demographic parameters (including mean age, gender, and diagnosis distribution) as well as preoperative examination findings, SAP measurements, and OCT results across the study groups*

	Group 1 (n=37)	Group 2 (n=27)	*p* value
Mean age (years)	73.4 ± 8.1	70.8 ± 7.3	0.187
Gender distribution (M/F)	24/13	15/12	0.451
Diagnosis (POAG/PEG)	21/16	14/13	0.697
IOP (Mean ± SD)	26.7 ± 7.1	28.6 ± 4.4	0.238
CCT (µm) (Mean ± SD)	526.8 ± 36.4	532.3 ± 41.2	0.775
Pigmentation in the iridocorneal angle [Median (min-max)]	3 (1-3)	3 (2-4)	0.558
C/D ratio (Mean ± SD)	0.69 ± 0.2	0.56 ± 0.3	0.110
Mean deviation (dB) (Mean ± SD)	-6.28 ± 6.8	-5.17 ± 4.9	0.137
mRNFLT (Mean ± SD)	66.54 ± 14.1	77.85 ± 17.1	0.010

CCT: central corneal thickness, IOP: intraocular pressure, mRNFLT: mean retinal nerve fiber layer thickness, M/F: male/female, PEG: pseudoexfloative glaucoma ,POAG: primary open angle glaucoma, SAP: standard automated perimetry, OCT: optical coherence tomography

Table 2: *Comparison of preoperative examination findings, SAP and OCT results between groups*

	Group 1 (n=37)	Group 2 (n=27)	*p* value
IOP (Mean ± SD)	26.7 ± 7.1	28.6 ± 4.4	0.238
CCT (µm) (Mean ± SD)	526.8 ± 36.4	532.3 ± 41.2	0.775
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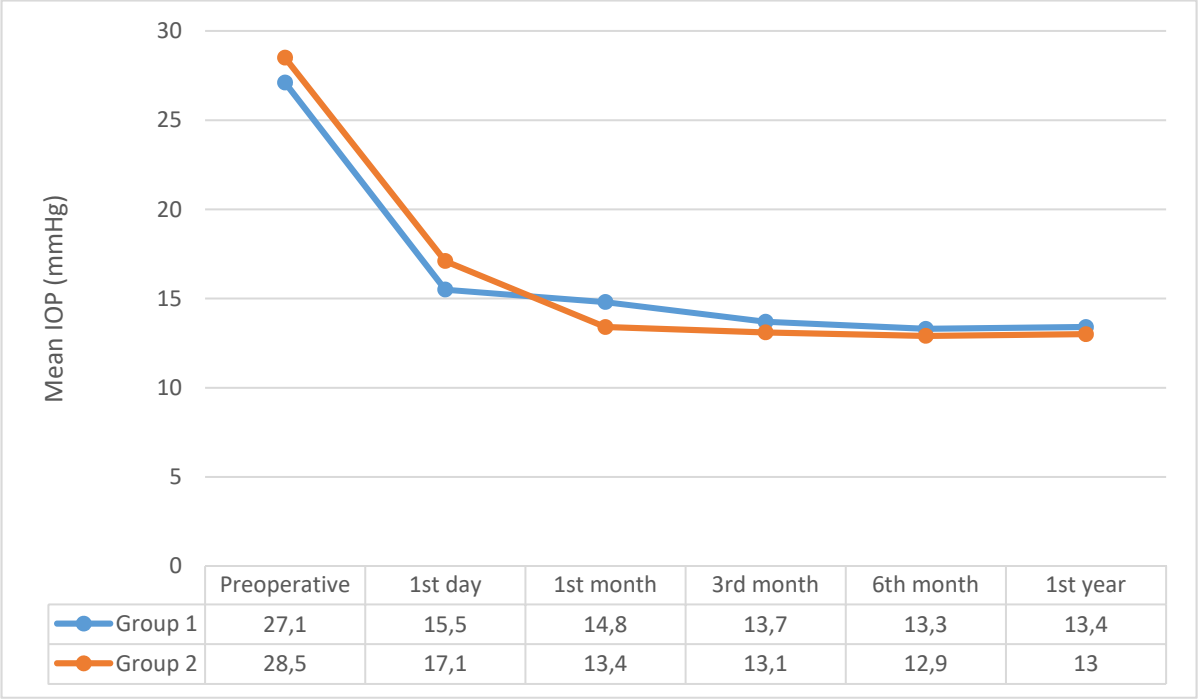
significant difference between the two groups in terms of central corneal thickness, degree of iridocorneal angle and degree of pigmentation at the iridocorneal angle. Preoperative mean cup/disc (c/d) ratio was similar between both groups (p=0.110), whereas mean mRNFLT was significantly lower in group 1 (p=0.011). The mean preoperative MD obtained with SAP was similar between the two groups (p=0.064). The mean number of anti-glaucomatous agents used preoperatively was 3.4 ± 0.2 in group 1 and 3.2 ± 0.1 in group 2 (p=0.416). The mean trabeculotomy extent achieved during GATT was 291.8 ± 77.6° in group 1 and 275.2 ± 81.8° in group 2; the difference was not statistically significant (p=0.464). Preoperative lens status did not differ significantly between the two groups, with 25 of 37 patients being phakic in the first group and 18 of 27 in the second group (p=0.940). In the overall cohort, 59.4% (n=38) of the patients underwent GATT procedure with phacoemulsification and 40.6% (n=26) underwent only GATT surgery. When only preoperative phakic patients (n=43) were analyzed, no difference was observed between the groups regarding the type of surgery performed, either GATT alone (n=3 in group 1 and n=2 in group 2) or GATT combined with phacoemulsification (n=22 in group 1 and n=16 in group 2) (p=0.929).

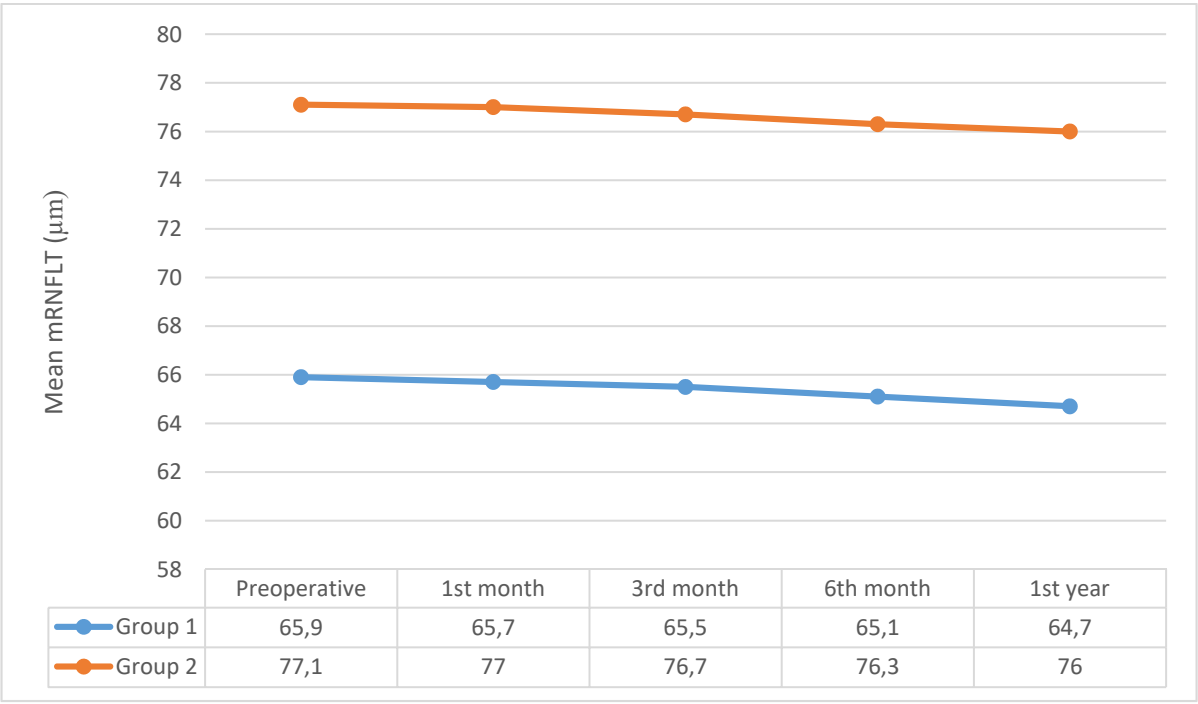
A transient and minor hyphema was observed in 48.4% (31/64) of the eyes. Of these, 93.5% (29/31) had spontaneous and complete resolution within a one week period. Both the incidence of hyphema development and the incidence of resolution within one week were similar in groups 1 and 2 (p=0.145 and p=0.265, respectively). One patient experienced vitreous haemorrhage, which also had complete and spontaneous resolution after five weeks. IOP spikes occured in five of 37 (13.5%) eyes in group 1 and six of 27 (22.2%) eyes in group 2. The mean durations of IOP spike were 3.5 ± 2.7 and 3.9 ± 2.3 days in group 1 and 2, respectively. Topical and systemic anti-glaucomatous agents were used for the management of the IOP spikes. In suitable cases, the administration of anti-glaucomatous agents was ceased once intraocular pressure had been successfully managed.

Mean IOP for both groups was significantly lower on postoperative day 1 and at all subsequent visits compared to the preoperative measurement (p<0.001 for both groups). There was no significant change in IOP for both groups in all postoperative measurements. At the first year, mean IOP was similar between the groups (p=0.410). The change in mean IOP over time is shown in Figure 1. The decrease in IOP values with time was similar in both groups (p=0.087). Although mean mRNFLT decreased during follow-up for both groups, the changes were not statistically significant (group 1, p=0.061; group 2, p=0.152). The change in mean mRNFLT measurements is shown in Figure 2. Similarly, for both groups, the mean MD measurements at preoperative and postoperative first year did not change significantly (group 1, p=0.243; group 2, p=0.345). At the first year, the mean number of anti-glaucomatous agents was 1.9±0.8 in group 1 and 0.4±0.2 in group 2, which was significantly different between the two groups (p=0.031). The number of anti-glaucomatous agents decreased significantly in both group 1 and group 2 at postoperative first year (group 1, p=0.021; group 2, p=0.013). The decrease in the number of anti-glaucomatous agents was significantly higher in group 2 compared to group 1 (p=0.032).



	Preoperative	1st day	1st month	3rd month	6th month	1st year
Group 1	27,1	15,5	14,8	13,7	13,3	13,4
Group 2	28,5	17,1	13,4	13,1	12,9	13

Figure 1: *Change in mean IOP in preoperative and postoperative follow-up in two groups*
IOP: intraocular pressure



	Preoperative	1st month	3rd month	6th month	1st year
Group 1	65,9	65,7	65,5	65,1	64,7
Group 2	77,1	77	76,7	76,3	76

Figure 2: *Change in mean oRSLTK measurements in two groups at preoperative and postoperative follow-up*
mRNFLT: mean retinal nerve fiber layer thickness

DISCUSSION

Glaucoma surgery indications and physician preferences change with each passing year. Trabeculectomy and tube shunt surgery are still important. However, new glaucoma surgeries[15], new cyclophotocoagulation protocols[16,17] and procedures developed with modifications of existing surgical techniques[18] are becoming preferable in some cases. New safe and effective glaucoma procedures are being studied to reduce the incidence of complications (particularly those related to blebs), shorten recovery time, and reduce the number of postoperative visits. In recent years, there have been numerous studies to evaluate the safety and efficacy of GATT surgery in various types of glaucoma.[19,20] However, there seem to be some shortcomings, especially regarding postoperative patient follow-up and mid to long-term outcomes of surgery. One of the most important issues is that there is not yet an accepted protocol for medical treatment in the postoperative period, and there are different approaches with the individual preferences of physicians. In order to overcome this deficiency, we evaluated the effect of sudden IOP increases and early discontinuation of anti-glaucomatous drugs on mid-term disease progression, which may be important in postoperative patient follow-up. In our study, it was observed that routine discontinuation of topical anti-glaucomatous agents after successful GATT surgery in PEG and POAG cases had no significant impact on disease progression at one-year follow-up.

In the literature, there are studies showing that the GATT procedure is an effective and safe surgery with predictable results in the treatment of glaucoma.[8,14,21,22] In 2014, Grover et al. reported the surgical technique and first results. [8] After this study, which showed a decrease in IOP of approximately 11 mmHg in one year follow-up, they reported a decrease in IOP of approximately 9 mmHg in 24 months follow-up.[14] In another study, it was shown that at least 20% decrease in IOP was achieved in POAG patients.[10] In some studies conducted with POAG and PEG patients, it has been reported that an average decrease in IOP between 21% and 65% was achieved after GATT or combined GATT-phacoemulsification.[20,23,24,25,26,27,28] According to the results of our study, similar to previous publications, IOP decreased by 46.81% and 55.24% at the end of the first year in patients with and without discontinuation of anti-glaucomatous agents, respectively. Also, in accordance with the literature, when all cases were evaluated together in our study, a 48.27% decrease in IOP was observed. It has been proven in many studies that the number of drugs used is significantly reduced after surgery.[8,14,25,27] Although the methodology of our study was different from previous studies, the number of anti-glaucomatous agents used was significantly decreased in both groups. Unlike in our study, anti-glaucomatous agents were routinely discontinued in group 2 in the postoperative period, but were restarted in the follow-up if needed.

In a study evaluating the second year results after combined phacoemulsification + GATT surgery in patients with intermediate-advanced POAG, a significant improvement in visual field MD measurements was reported.[29] In our study, although there was a significant decrease in IOP at one-year follow-up, there was no significant change in MD. The improvement in visual field in the previous study seems to be related to the simultaneous phacoemulsification surgery in all cases. In a multicenter study, one-year results after GATT + phacoemulsification were analysed in patients with POAG at different stages and no change in visual field MD was reported.[30] The results of our study seem to be compatible with the few studies in terms of visual field MD. In the literature, there is only one study in which RNFLT was evaluated. It was shown that there was no change in RNFLT in 37 patients with PEG or POAG in the first year after GATT.[31] Although a similar result was observed, our study more reliably demonstrates that the optic nerve is anatomically preserved after GATT since there were 64 patients in our study. More importantly, the effect of postoperative discontinuation of anti-glaucomatous agents on progression was analysed for the first time in the literature and no effect on disease progression was observed. Glaucomatous therapy discontinuation after successful GATT surgery may be a better choice in mild and moderate glaucoma cases because when the aqueous outflow continues, it may prevent obstruction of the reopened outflow pathway.

Limitations of the study

The most important limitation of our study is its observational retrospective design. Another limitation seems to be that the decision of whether to discontinue postoperative anti-glaucomatous agents was not randomised but was determined by the surgeon's personal preference. However, it should be kept in mind that there is no consensus regarding postoperative patient follow-up and the primary aim of

our study was to investigate this issue. Another limitation of this study is its retrospective nature, which led to the inclusion of cases operated on by two different surgeons. Although both surgeons were experienced in glaucoma surgery, the involvement of multiple surgeons may have introduced variability in surgical technique and outcomes, potentially affecting the consistency of the results.

CONCLUSION

There is still no consensus in the literature regarding postoperative follow-up after GATT surgery. In our study, we analysed the mid-term anatomical and functional results of open angle glaucoma patients who underwent successful GATT or GATT + phacoemulsification surgery to evaluate the effect of postoperative anti-glaucomatous discontinuation on progression. Postoperative anti-glaucomatous agents were continued in some patients and discontinued in the other group due to the surgeon's personal preference. One-year follow-up showed no difference in IOP measurements and no anatomical or functional progression of the disease in both groups. In conclusion, the results of our study show that discontinuation of anti-glaucomatous agents in the postoperative period after successful GATT or GATT + phacoemulsification surgery has no effect on IOP and disease progression in patients with open angle glaucoma. It should be kept in mind that some cases may require the use of anti-glaucomatous agents again and postoperative follow-up should be performed appropriately. It would be appropriate to conduct prospective randomised controlled studies in order to establish an algorithm for the follow-up of patients after GATT surgery, which is becoming increasingly common today.

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