



Factors Affecting the Incidence of Ptosis after Trabeculectomy

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Abstract

Objectives: The aim of this study was to investigate the incidence of postoperative ptosis after primary trabeculectomy and the possible factors contributing to ptosis.

Materials and Methods: A total of 312 patients (339 eyes) who underwent trabeculectomy with mitomycin-C between 2015 and 2020 were retrospectively evaluated. Patients who had regular follow-up for at least 6 months and no history of ptosis or ptosis surgery were included. Age, sex, glaucoma type, preoperative and postoperative intraocular pressure, preoperative and postoperative antiglaucoma medications, number of antiglaucoma drops, duration of antiglaucoma medication use, history of eye itching due to antiglaucoma medication-associated allergy, duration of follow-up, postoperative needling, needling time, and ocular massage were recorded. Ptosis was defined as ≥ 2 mm reduction in margin-reflex distance 1 from preoperative levels. Ptosis that had not improved for at least 6 months was considered persistent ptosis. Multivariate logistic regression was used to determine potential predictors of ptosis development.

Results: Ptosis after trabeculectomy was observed in 35 of 339 eyes (10.3%). Thirty eyes of 30 patients (8.8%) had transient ptosis and 5 eyes of 4 patients (1.5%) had persistent ptosis. Preoperative duration of antiglaucoma medication use, drug(s) used (prostaglandin analogs, beta-blockers, alpha-2 agonists, carbonic anhydrase inhibitors, or combinations of these), needling time, and ocular massage after trabeculectomy did not differ significantly between groups ($p>0.05$). Needling and eye itching due to antiglaucoma medication-associated allergy were significantly higher in patients with ptosis ($p<0.05$).

Conclusion: Ptosis after trabeculectomy is an important problem for glaucoma patients. It has been observed that needling and a history of eye itching due to antiglaucoma drug-associated allergy may increase the risk of ptosis.

Keywords: Medication-associated allergy, glaucoma, needling, ptosis, trabeculectomy

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Introduction

In the literature, the incidence of ptosis following intraocular surgery is reported to be 10-11.4%.^{1,2} Despite its high frequency, ophthalmologists underestimate the impact of this complication on patients' quality of life. Postoperative ptosis is a multifactorial condition that may develop transiently due to eyelid edema, eyelid or intraorbital hematoma, ocular inflammation, and neurogenic causes, but persistent ptosis can also occur as a result of dehiscence or disinsertion of the levator aponeurosis.^{3,4,5} Although it often improves within months of surgery, ptosis may be permanent and require corrective surgery. This complication is reported to be more common after glaucoma surgery than after other anterior segment surgeries.²

Trabeculectomy is one of the most common glaucoma surgeries in the world. Ptosis after trabeculectomy has been reported at rates between 8% and 19%.^{6,7,8,9,10} The higher rate may be related to the effect of manipulations performed to create adequate surgical space during trabeculectomy or to chronic bleb irritation.² Ptosis can severely impair quality of life in glaucoma patients, causing astigmatism and impairing vision by increasing existing visual field defects, and it also makes it difficult to measure intraocular pressure (IOP) by applanation tonometry.^{7,8,9,10,11} It is important to know the risk factors and take precautions in glaucoma patients, as well as to inform patients about this issue before trabeculectomy.

The present study aimed to investigate the incidence and possible risk factors of ptosis after trabeculectomy, a filtration surgery.

Materials and Methods

The medical records of 339 eyes of 312 patients who underwent trabeculectomy with antimetabolite were retrospectively reviewed. Patients who were followed up and surgically treated by the same ophthalmologist (E.M.S.) in both the glaucoma and oculoplastic surgery clinics between January 2015 and May 2020 were included. The study was conducted in accordance with the tenets of the Declaration of Helsinki and received ethics committee approval. Written informed consent form was obtained from the patients whose images were used.

We included patients who had been followed up regularly for at least 6 months after trabeculectomy. Exclusion criteria included inadequate documentation, history of ptosis or ptosis surgery, history of intraocular surgery within 6 months, and combined surgeries. All patients were white.

The following data were obtained from the patients' medical records: age, sex, pre- and postoperative IOP, glaucoma type (primary open angle glaucoma, pseudoexfoliation glaucoma, primary angle closure glaucoma, or secondary glaucoma), antiglaucoma drug used preoperatively (prostaglandin analogs [PGA], beta-blockers, alpha 2 agonists, carbonic anhydrase inhibitors, or combinations thereof), number of antiglaucoma drops, the duration of antiglaucoma medication use, history of eye itching due to antiglaucoma medication-associated allergy, duration of follow-up, whether needling was done

after trabeculectomy, needling time, and ocular massage, and ptosis (transient or persistent). Ptosis was defined as a ≥ 2 mm decrease in margin-reflex distance 1 (MRD1), and patients with upper eyelid defect in visual field test were included. Ptosis that developed after trabeculectomy and resolved spontaneously within 6 months was considered transient ptosis. Ptosis that lasted more than 6 months was classified as persistent ptosis.

All procedures (trabeculectomy and ptosis surgery) were performed by one experienced surgeon (E.M.S.). All patients underwent trabeculectomy with mitomycin C (MMC) under sub-tenon local anesthesia using the same surgical instruments and technique and only a corneal traction suture. Fornix-based conjunctival incisions with square scleral flaps were made and 0.2 ng/mL MMC was applied beneath the scleral flap for 2 minutes. The scleral flap was made in the superior nasal quadrant. Follow-up examinations were scheduled by the same ophthalmologist at postoperative 1, 2, and 7 days; 2, 4, 6, and 8 weeks; 3, 6, 9, and 12 months, and every 4-6 months thereafter.

In case of increased IOP and decrease in bleb height, ocular massage was performed by the bleb with a cotton-tipped applicator under slit-lamp biomicroscopy. The massage was continued until swelling of the bleb and dispersion of aqueous humor under the conjunctiva was observed. A speculum was not placed for this procedure. Patients were taught how to do ocular massage over the lower eyelid and were advised to perform it nightly before sleeping while looking up. The bleb was evaluated 1 week later to determine whether to continue the ocular massage. Needling was performed in the operating room by the same surgeon using a sterile surgical drape and speculum.

Statistical Analysis

Statistical analyses were performed with IBM SPSS Statistics version 22.0 (IBM, Armonk, NY, USA). Categorical data were presented as frequency and percentages and continuous data were presented as the mean \pm standard deviation. The Shapiro-Wilk's test and histograms were used to evaluate for normal distribution of the data. In the comparison between groups with and without ptosis, parameters with normal distribution were evaluated with the independent samples t-test, and those without normal distribution were evaluated with the Mann-Whitney U test. For categorical variables, the chi-square test was used. Multivariate logistic regression was used to determine potential predictors of ptosis development for variables with a p value ≤ 0.20 . A p value 0.05 was considered statistically significant.

Results

A total of 339 eyes of 312 patients that underwent trabeculectomy with MMC were retrospectively included in this study. The total number of eyes with ptosis was 35 (10.3%). Transient ptosis was observed in 30 eyes (8.8%) and persistent ptosis in 5 eyes (1.5%). All cases of ptosis were aponeurotic; none of the patients had levator dysfunction. **Figure 1A** shows a patient with left aponeurotic ptosis 6 months after trabeculectomy with inferior and superior arcuate defects in the visual field. **Figure 1B** shows the visual field assessed after

lifting the left eyelid, demonstrating that the patient will benefit from ptosis surgery. **Figures 1C and 1D** show photographs before and after ptosis surgery, respectively.

The patients' characteristics are presented in **Table 1**. There were no statistical differences between patients with and without ptosis after trabeculectomy in terms of mean age ($p=0.91$), sex ($p=0.38$), or duration of follow-up ($p=0.06$). IOP did not differ significantly between the groups.

The patients' glaucoma types, antiglaucoma medication usage, needling rate and timing, ocular massage, and history of eye itching are summarized in **Table 1**. Needling after trabeculectomy and history of eye itching due to antiglaucoma medication-associated allergy were considered clinically significant factors associated with increased ptosis. Needling was performed once in this study. The mean time between trabeculectomy and needling was 4.6 ± 1.3 weeks in the patients with ptosis and 5.9 ± 1.7 weeks in the patients without ptosis ($p=0.18$). None of the patients had postoperative procedures such as laser suture lysis, bleb revision, or compression suture. Levator aponeurosis advancement was performed within a year in all patients with persistent ptosis. No bleb failure was observed after ptosis surgery.

Multivariate logistic regression was used to identify potential and final predictors of ptosis development after trabeculectomy. When age, sex, eye itching, postoperative ocular massage, needling, needling time, and PGA use were evaluated in multivariate logistic regression analysis, only preoperative history of eye itching due to antiglaucoma medication-associated allergy (odds ratio [OR]=2.52, 95% confidence interval [CI]: 0.032-0.202, $p=0.0001$) and needling (OR=1.41, 95% CI: 0.098-0.608, $p=0.002$) were found to be predictive of ptosis development (**Table 1**).

Discussion

In the present study, we investigated the incidence of ptosis after trabeculectomy and the factors that may be associated with this complication. In order to avoid the possible influence of surgeons and surgical techniques on outcomes, we included only patients operated on by the same surgeon with the same technique and surgical instruments. Combined surgeries were excluded to evaluate only the effect of trabeculectomy. In this study, the incidence of ptosis after trabeculectomy was 10.3%, which is comparable to previous studies (8-19%).^{6,7,8,9,10} The incidence of persistent ptosis was 1.5%. We determined that eye

Table 1. Univariate and multivariate regression analysis of factors associated with ptosis after trabeculectomy

Parameters	Ptosis (34 patients, 35 eyes)	No ptosis (278 patients, 304 eyes)	Univariate analysis p-value (95% CI for OR)	Multivariate analysis p-value (95% CI for OR)
Age (years)	62.0±16.3	63.09±15.1	0.686 (0.982-1.028)	0.91 (0.531-20.738)
Sex (n female/male)	17/18	171/133	0.388 (0.676-2.743)	0.38 (0.901-1.057)
Duration of follow-up (months)	27.8±17.4	34.3±20.2	0.072* (0.998-1.037)	0.325 (0.965-1.112)
Preop IOP (mmHg)	22.3±10.9	23±6.7	0.925 (0.908-1.112)	
Postop IOP (mmHg)	13.0±2.9	11.7±2.5	0.287 (0.572-1.180)	
Glaucoma type (%)				
POAG	31.4	21.1	0.388 (0.046-3.241)	
PXG	42.9	51.0	0.689 (0.085-5.583)	
PACG	2.9	3.6	0.733 (0.041-13.050)	
Secondary	22.9	24.4	0.411 (0.046-3.712)	
Number of preop antiglaucoma medications	2.24±0.7	2.23±0.7	0.983 (0.569-1.781)	
Preop duration of antiglaucoma medication use (months)	12.5±6.6	13.4±9.8	0.243 (0.990-1.109)	
Antiglaucoma drug used (%)				
PGA	28.6	41.0	0.155* (0.266-1.235)	0.544 (0.460-4.370)
Beta-blocker	42.3	39.1	0.264 (0.328-1.357)	
Carbonic anhydrase inhibitor	40.8	47.3	0.332 (0.698-2.902)	
Alpha-2 agonist	53.2	51.1	0.658 (0.423-1.722)	
Preop history of eye itching due to antiglaucoma medication-associated allergy (%)	54.3	6.6	0.0001* (7.540-37.713)	0.0001** (9.803-73.528)
Postop ocular massage (%)	22.9	13.3	0.134* (0.818-4.535)	0.71 (0.193-3.067)
Postop needling (%)	62.9	20.7	0.0001* (3.085-13.565)	0.002** (0.098-0.608)
Postop needling time (weeks)	4.6±1.3	5.9±1.7	0.288 (0.890-1.479)	

Data are expressed as mean ± SD or percentage of eyes. IOP: Intraocular pressure, Preop: Preoperative, Postop: Postoperative, POAG: Primary open angle glaucoma, PXG: Pseudoexfoliation glaucoma, PACG: Primary angle closure glaucoma, PGA: Prostaglandin analog, OR: Odds ratio, CI: Confidence interval, SD: Standard deviation * $p \leq 0.20$, ** $p < 0.05$, significant results are shown in bold

itching due to allergy to antiglaucoma medication and needling might be related to the development of ptosis. Patients with and without ptosis showed no significant differences in age, sex, duration of follow-up, glaucoma type, antiglaucoma medication number and duration of use, type of antiglaucoma agent, or ocular massage.

There are few prospective studies in the literature reporting ptosis after trabeculectomy.^{7,8} Jampel et al.⁸ reported that ptosis after trabeculectomy is one of the most important postoperative complications and had an incidence of 12% in the first month. However, ptosis was assessed subjectively, and the prevalence of ptosis at 6 months was not reported.⁸ The mean follow-up time of the ptosis group in our study was 28 months. In another prospective study, the incidence of ptosis after trabeculectomy with MMC performed by the same surgeon using the same technique was reported to be 19%.⁷ Naruo-Tsuchisaka et al.⁷

reported that the mean follow-up time was only 6 months, and argued that the presence of an intraoperative traction suture in the peripheral cornea or a postoperative procedure (laser suture lysis, needling, transconjunctival scleral flap suture, or compression suture) did not affect the incidence of ptosis. In addition, the reason for the higher rate compared with other studies was not reported.⁷ Among retrospectively designed studies, the incidence of ptosis after trabeculectomy was 10.7% in a study by Song et al.⁹ and 12.5% in a study by Fukushima et al.¹⁰ According to Song et al.,⁹ there was no association between ptosis and cataract surgery, type of conjunctival flap, or previous ocular surgery, but the role of antiglaucoma drugs or any information about the surgeons were not reported. In our study, we included only trabeculectomy procedures to standardize the operation time. Fukushima et al.¹⁰ reported that deepening of the upper eyelid sulcus (DUES) may be an important predictor of ptosis after trabeculectomy and that

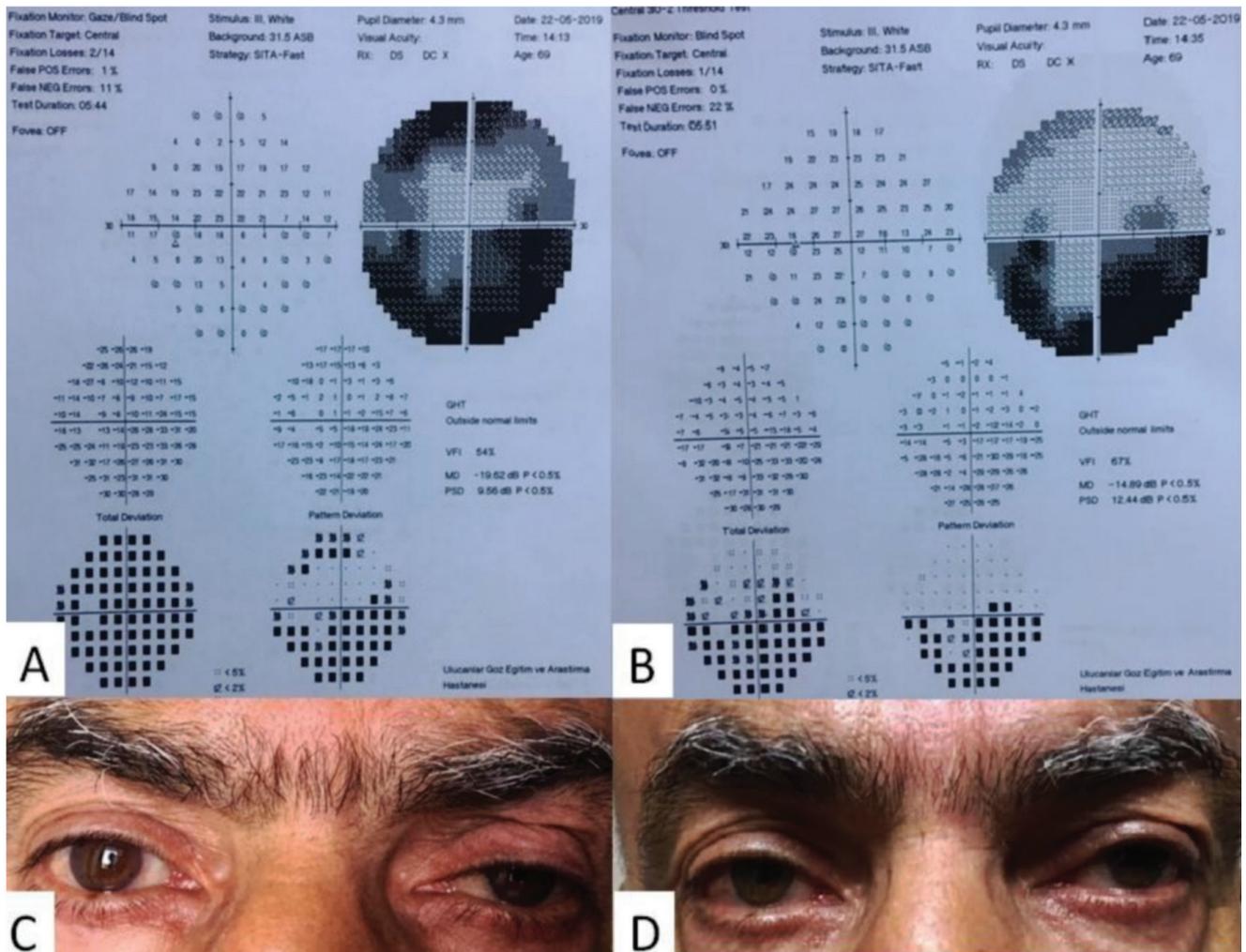


Figure 1. Evaluation of a 69-year-old male patient who had persistent ptosis on following trabeculectomy. A) Superior and inferior arcuate defects were detected on visual field after trabeculectomy. B) The visual field test was repeated 15 minutes later while lifting the left eyelid. On the second test, the inferior arcuate defect (associated with glaucoma) remained while the superior visual defect (due to ptosis) was absent. This indicated that ptosis surgery would benefit the patient and significantly improve his quality of life. C) Left persistent ptosis after trabeculectomy (MRD1: 1 mm). D) The left upper ptosis improved after levator aponeurosis advancement
MRD1: Margin-reflex distance 1

there was no difference between the ptosis and non-ptosis groups in terms of glaucoma types, number of antiglaucoma drugs, or postoperative needling times.

In addition, traction of the levator muscle complex by bridle sutures or forceps, eyelid speculum, and excessive infraduction may increase the rate of ptosis after trabeculectomy.^{5,12} We chose corneal traction sutures and the same surgical instrumentation for all procedures. Many factors have been investigated in all these studies, but there is no clear consensus on the risk factors for this important complication. This may be attributable to the preference of different surgical techniques and surgical instruments, different surgeons, or different follow-up approaches.

Chronic eye itching is one of the known causes of aponeurotic ptosis.¹³ Trauma to the levator muscle complex due to eye itching or ocular massage may lead to easier detachment of the already weakened aponeurosis in patients undergoing trabeculectomy. Manipulation of the bleb by needling is another procedure that may cause trauma to the levator complex in these patients. A comparison of the aforementioned factors has not been published in the literature. In our study, a higher rate of ptosis was observed in patients with needling and eye itching. Although needling is a short procedure, eyelid edema, minor trauma from the procedure or the blepharostat, and inflammation may have caused ptosis. In addition to the trauma to the levator aponeurosis during trabeculectomy, these mechanisms might have contributed to the development of ptosis. Needling was performed 4-5 weeks after trabeculectomy in our study and may cause a second separation of the levator aponeurosis, which was already traumatized during trabeculectomy. Any intervention in the early period after trabeculectomy can cause further separation of the aponeurosis. In patients with ptosis, the time between surgery and needling was approximately 1.3 weeks earlier than in those without ptosis. However, this difference did not prove to be statistically significant.

The development of an allergic reaction to antiglaucoma medication results in eye redness, dryness, tearing, chronic irritation, and eye itching.^{14,15,16,17,18} In such cases, the patient is expected to cause mechanical eyelid trauma. To our knowledge, there are no data on ptosis associated with a history of allergy to antiglaucoma medication. Eyelid rubbing due to an allergic reaction may cause aponeurotic ptosis in patients who either exert excessive force on their eyelids or have an intrinsically weak levator aponeurosis. Itching may also be considered a minor and persistent trauma. Although the type of glaucoma drug used was not associated with the development of ptosis in our study, the literature data indicates that most allergies are caused by the alpha-2 agonist and PGA groups.^{14,15,16,17,18} In patients with eye itching caused by an allergy to topical antiglaucoma medication, it should be replaced with another antiglaucoma drug known to be less allergenic, and treatment with both topical and oral antiallergic drugs should be provided depending on symptom severity.

Ocular massage is a simple technique used to treat early bleb failure after trabeculectomy. Although no significant difference was found between the groups with and without ptosis in our study, these patients should be advised to be careful with massage.

One of the most preferred agents in glaucoma treatment is PGAs, but they are associated with many side effects involving the ocular appendages. Prostaglandin-associated periorbitopathy (PAP) has been reported after the use of PGA and includes eyelid pigmentation, eyelash changes, dermatochalasis, orbital fat atrophy, enophthalmos, narrow orbit, levator dysfunction, DUES, and ptosis.^{19,20,21} In addition, a possible association between PGA exposure and failure of ptosis surgery has been reported.²² In the study by Fukushima et al.,¹⁰ PGA was used in all cases in both the blepharoptosis and non-blepharoptosis groups, but other antiglaucoma drugs were not discussed. In our study, no significant difference was found between the use of PGA and other antiglaucoma agents (beta-blockers, alpha-2 agonist, and carbonic anhydrase inhibitors) in the development of ptosis. The reason for this could be the high awareness of PAP and the replacement of PGA with another agent as soon as DUES is noticed. It is very important to keep in mind the periorbital side effects of PGA use and ensure glaucoma specialists are aware of this issue.

Study Limitations

Although this study evaluated a large number of parameters in 339 eyes after trabeculectomy, it has several limitations. Firstly, it was a retrospective study. Another limitation is that we did not evaluate bleb morphology and characteristics or DUES, which may be risk factors for ptosis. A prospective study investigating the influence of bleb morphology would certainly be beneficial. Because of the shortcomings of this study, we are conducting a prospective study examining these parameters. The strengths of this study are that all trabeculectomy procedures were performed by the same surgeon using the same technique and surgical instruments, and we evaluated many factors such as age, sex, glaucoma type, preoperative antiglaucoma drug use, ocular itching associated with antiglaucoma treatment, duration of follow-up, and postoperative needling, needling time, and ocular massage. Moreover, transient and persistent ptosis were evaluated separately. The mean duration of follow-up was long, at 31.05 months.

Conclusion

This study reports the incidence and factors contributing to ptosis after trabeculectomy. It is well known that ptosis is one of the most important complications after trabeculectomy. According to our findings, preoperative ocular itching due to allergies to antiglaucoma medications and postoperative needling may increase ptosis after trabeculectomy. We recommend raising awareness of related factors to prevent ptosis, which affects the quality of life of glaucoma patients.

Ethics

Ethics Committee Approval: University of Health Sciences Türkiye, Ankara Training and Research, Hospital, E-21-619.

Informed Consent: Written informed consent was obtained from the patient whose images were used.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: E.M.Ş., Concept: K.S.C., E.M.Ş., Design: K.S.C., E.M.Ş., Data Collection or Processing: K.S.C., E.M.Ş., Analysis or Interpretation: K.S.C., E.M.Ş., Literature Search: K.S.C., E.M.Ş., Writing: K.S.C., E.M.Ş.

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