ORIGINAL ARTICLE

The Effect of Exfoliation on Surgically Induced Astigmatism in Patients After Trabeculectomy

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ABSTRACT

Purpose: Our aim was to compare the effects of exfoliation (XF) on surgically induced astigmatism (SIA) in patients with primary open-angle glaucoma (POAG) and exfoliation glaucoma (XFG) after trabeculectomy.

Materials and Methods: Twenty-one eyes with POAG and 22 eyes with XFG were included in this prospective clinical study. The eyes had uncomplicated initial trabeculectomy with 5-fluorouracil (5-FU). All cases underwent a complete ocular examination including corneal topography at baseline and at postoperative first, third, and sixth months. SIA was calculated by the vector analysis method using the Holladay-Cravy-Koch formula.

Results: The mean SIA values were 0.92±0.35 diopter (D), 0.96±0.34 D, and 0.82±0.34 at the first, third, and sixth months, respectively, in the POAG group and 1.17±0.43 D, 1.25±0.44 D, and 1.05±0.42 D at the first, third, and sixth months, respectively, in the XFG group. Significant differences existed between the groups at postoperative first and third months, but no significant difference was observed at the sixth month (p=.040, p=.027, p=.061, respectively). At the sixth month, with the rule (WTR) astigmatism rates were 76% in the POAG group and 45% in the XFG group (p=.039). Significant correlations were found between the SIA values, and intraocular pressure changes were observed at the first and sixth months (r=-0.502, p=.017; r=-0.520 p=.013) in the XFG group.

Conclusion: SIA values in XFG patients after trabeculectomy were higher in the early period compared to POAG patients. This may be due to local inflammation caused by XF and its effect on corneal biomechanics.

Key words: Trabeculectomy, Surgically induced astigmatism, Primary open-angle glaucoma, Exfoliation glaucoma, Exfoliation.

INTRODUCTION

Trabeculectomy, which remains the golden standard of glaucoma surgery, has many serious complications such as hypotonous maculopathy, choroidal effusion, cataract formation, and long-term bleb-related infections.[1,2] Trabeculectomy might also cause some changes in anterior segment morphology postoperatively because of decreased intraocular pressure (IOP) and/or bleb formation.[3-6] These morphological alterations induce surgically induced astigmatism (SIA), which depends on such factors as the surgical technique, including the scleral flap size, localization and sutures, antimetabolite use, excessive cauterization, posteriorly placed wound gape, and factors related to wound healing.[7-13]

The prognosis of exfoliation glaucoma (XFG) is worse because it has higher IOP and fluctuations than primary open angle glaucoma (POAG).[14] Exfoliation (XF) has been shown to alter corneal biomechanics.[15,16] There are also studies showing increased local and systemic inflammation in XF patients.[17,18] For these reasons, it can be predicted that SIA after trabeculectomy in XFG patients will be different than POAG patients. The aim of our study was to investigate the changes caused by XF in SIA after trabeculectomy.

MATERIALS AND METHODS

Twenty-one eyes of 21 cases with POAG and 22 eyes with XFG were included in this prospective clinical study. The eyes had an uncomplicated trabeculectomy with 5-fluorouracil (5-FU) between May 2014 and September 2015 at Ulucanlar Eye Research Hospital. Despite receiving maximum tolerated medical treatment, the patients had uncontrolled glaucoma. All of the study procedures were

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conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from each participant. This study was approved by The Ethical Committee of Numune Training and Research Hospital.

The best corrected visual acuities, biomicroscopic and fundus examinations, IOP values measured by Goldmann applanation tonometer, central corneal thickness (CCT) measurements, visual field measurements (Humphrey automated perimeter) and retinal nerve fiber thickness were recorded in all patients. POAG patients were diagnosed according to the presence of glaucomatous visual field defect, IOP>22 mmHg, open angle and glaucomatous optic nerve damage. XFG cases were diagnosed by observing exfoliation material on biomicroscopic examination. The inclusion criteria were POAG or XFG patients older than 40 years and patients requiring trabeculectomy cause of insufficient response to medical treatment. Patients with angle closure glaucoma, patients younger than 40 years old, glaucoma types other than POAG and XFG and patients with early trabeculectomy complications were excluded. We also excluded eyes with spherical equivalent (SE) values > ±6.0 diopter (D).

Corneal topography (Pentacam HR-Scheimpflug imaging system, Oculus, Weltzar, Germany) was performed preoperatively and at the first, third, and sixth postoperative months. SIA was calculated by the vector analysis method using the Holladay-Cravy-Koch formula.[19]

Surgical technique

All surgeries were performed by the same experienced surgeon (UE) after using sub-Tenon’s anesthesia (with lidocaine hydrochloride 20 mg/ml). A fornix-based conjunctival flap was prepared superiorly. After dissecting the conjunctiva and the Tenon’s capsule, a thin cellulose sponge (approximately 5x10 mm) soaked with 5-FU (50 mg/ml concentration) was placed between the conjunctival Tenon’s capsule flap and the sclera for five minutes without any contact with the limbus or cornea. During this procedure, the cornea was covered with methylcellulose. After irrigating the 5-FU with sterile BSS solution, one-half thickness approximately 4x4 mm square scleral flap was dissected. Then a trabeculectomy (approximately 2x2 mm) and a peripheral iridectomy was performed. The corners of the scleral flap were closed with 10-0 nylon sutures. The conjunctiva and Tenon's capsule was closed on the scleral flap with 8-0 vicryl. Postoperative topical antibiotics (Vigamox® 0.5% Ophthalmic Solution Alcon) 4x1 (1 month) and topical steroid (Predforte® 1% Ophthalmic Solution Allergy) 4x1 (2 months) and cyclopentolate 2x1 (2 weeks) were used.

Statistical Analysis

Descriptive statistics were given as mean±standard deviation. Chi-square test was used for categorical variables and Wilcoxon and Mann Whitney U tests were used for dependent and independent continious variables. P <0.05 was considered statistically significant. Analyzes were performed using SPSS software package version 20.0 (IBM, Armonk, NY).

RESULTS

The mean age of 11 (52.3%) male and 10 (47.7%) female POAG cases was 59.4±8.4 (44-74 years) years. The mean age of 10 (45.5%) male and 12 (54.5%) female XFG cases was 59.6±8.3 (45-73 years) years. There was no difference between the groups in terms of age and gender.(sex: p=0.763, age: p=0.961). Table 1 summarizes the preoperative visual acuity, SE, and IOP values of the groups. The mean SE changed from -1.86±1.31 D (baseline) to -1.26±1.55 D at the sixth month in patients with POAG (p<.001). Also, a significant difference was observed between baseline (-1.54±1.72 D) and postoperative sixth months (-0.84±1.90 D) SE values of the XFG group (p=0.05). The preoperative visual acuity changed from 0.30±0.16 to 0.27±0.15 in POAG (p=0.912) and from 0.19±0.12 to 0.17±0.12 in XFG (p=0.922) at the sixth postoperative month.

Table 2 summarizes the mean SIA values. In the POAG group, the SIA values were 0.92±0.35 D, 0.96±0.34 D, and 0.82±0.34 D at the first, third, and sixth postoperative months, respectively. In the XFG group, the SIA values were 1.17±0.43 D, 1.25±0.44 D, and 1.05±0.42 D at the first, third, and sixth postoperative months, respectively. At the first and third months, significant differences were found between the groups but it was insignificant at the sixth month (p=0.040, p=0.027, p=0.061, respectively)

Table 1. *The demographic and clinical baseline characteristics.*

	POAG	XFG
Number of eyes	21	22
Age (years)	59.4±8.4	59.6±8.3
Male/female	11/10	10/12
Preop. Visual acuity (logMAR)	0.30±0.16	0.19±0.12
Preop IOP (mmHg)	30.9±4.6	33.7±6.9
Mean SE (D)	-1.86±1.31	-1.54±1.72

POAG: Primary open-angle glaucoma, **XFG:** Exfoliation glaucoma, **Preop:** Preoperative, **IOP:** Intraocular pressure **SE:** spherical equivalent, **D:** Diopter

Table 2. *Postoperative surgically-induced astigmatism values of the groups.*			
	Postop first month	Postop third month	Postop sixth month
POAG	0.92±0.35 D	0.96±0.34 D	0.82±0.34 D
XFG	1.17±0.43 D	1.25±0.44 D	1.05±0.42 D
P value	0.040*	0.027*	0.061

POAG: Primary open-angle glaucoma, **XFG:** Exfoliation glaucoma, **Postop:** Postoperative, **D:** Diopter
*Statistically significant

(Table 2).

In the POAG group, 16 eyes (76%) had with the rule (WTR) astigmatism and five eyes (24%) had against the rule (ATR) astigmatism at the sixth month. However, in the XFG group, 10 eyes (45%) had WTR and 12 eyes (65%) had ATR astigmatism at the sixth month. The difference between the groups was significant (p=0.039) (Table 3).

No significant difference was found between the POAG and XFG groups in terms of preoperative IOP (p=0.242). The mean IOP decreased from 30.9±4.6 mmHg to 17.1±3.1, 17.5±2.5, and 17.4±2.5 mmHg values at the postoperative first, third, and sixth months, respectively, in the POAG group (p<.001 for all). In the XFG group, the preoperative IOP was 33.7±6.9 mmHg, which decreased to 16.2±4.0 mmHg, 16.4±3.2 mmHg, and 16.2±2.9 mmHg at the postoperative first, third, and sixth months, respectively (p<0.001 for all). The decrease in IOP was significantly higher in the XFG group at one month than at six months (p=0.039, p=0.059, respectively). None of the cases in our study used any anti-glaucoma agent within the postoperative six months. At the first and sixth postoperative months, significant correlations existed between the SIA values and IOP changes in the XFG group (r=-0.502, p=0.017) (r=-0.520, p=0.013). However, no significant correlations existed in the POAG group (r =-0.355, p=0.114) (r = -0.389, p=0.081).

Table 3. *With the rule and against the rule astigmatism rates at the sixth postoperative month.*			
	POAG (n / %)	XFG (n / %)	P value
WTR	16 (76%)	10 (45%)	0.039*
ATR	5 (24%)	12 (65%)	

POAG: Primary open-angle glaucoma, **XFG:** Exfoliation glaucoma, **WTR:** With the rule, **ATR:** Against the rule
*Statistically significant

DISCUSSION

Trabeculectomy, the golden standard of glaucoma surgery, causes a non-physiological flow of humor aqueous (HA) related with its bleb formation, which is often related to SIA, postoperative morphological anterior segment alterations, and decreased IOP.[1-8] We examined cases of POAG and XFG who had trabeculectomy with 5-FU because of inadequate medical treatment for uncontrolled glaucoma. Our main goal was to compare the effect of XF on SIA after trabeculectomy. To the best of our knowledge, no previous reports have compared trabeculectomy induced SIA between POAG and XFG patients.

The factors affecting SIA in trabeculectomy are the location of the incision, its width, and the biomechanical properties of the cornea (such as CH).[7-13,15,16] Claridge et al.[20] suggested that the intensity of scleral cauterization, large drainage blebs and postoperative ptosis contributed to corneal astigmatic change. In this study, it was reported that postoperative IOP and surgical site had independent effects on SIA. Therefore, SIA is inevitable because of these changes after a trabeculectomy, as found in our patients.

Many previous studies have reported the relation between SIA and glaucoma surgery. In their recent study, Delbeke et al.[7] investigated the effect of a primary trabeculectomy with a fornix-based conjunctival flap with mitomycin C on astigmatism. They observed a statistically significant shift in astigmatism WTR six months after a trabeculectomy without a significant postoperative difference in SE values.[7] Conversely, Kook et al.[3] performed a trabeculectomy with a limbus-based conjunctival flap with mitomycin C and followed up with their patients for one year. They observed WTR astigmatism up to three months and an ATR shift between three and 12 months. They observed a slower and long-lasting ATR shift until one year.[3] We also performed a trabeculectomy with a fornix-based conjunctival flap; however, unlike the two abovementioned studies, we used 5-FU. Different from Delbeke et al.'s study, we observed significant differences in the SE values in our cases. We observed WTR astigmatism in 48.8% and ATR astigmatism in 51.2% of our patients in both groups at the postoperative sixth month. Hong et al.[8] investigated the effect of mitomycin C on SIA and observed less WTR astigmatism and a continuous ATR shift until 12 months in the mitomycin C group compared with their cases without anti-metabolite use.

We included POAG and XFG cases in our study to investigate the effects of the presence of exfoliation in all of the tissues of the eye or other characteristics of XFG on these postoperative astigmatic changes. As exfoliation material aggregates on the corneal endothelium and causes a reduced number of endothelial cells, it seems reasonable that it might affect corneal astigmatism.[21] More complications of a trabeculectomy might occur in cases of XFG than POAG because of higher preoperative IOP values, increased inflammation and fibrinous reaction, and the risk of hemorrhage due to the iris vasculopathy.[21] Not only the endothelial layer but other corneal layers such as the subbasal nerve plexus and Descement's membrane can be affected by pseudoexfoliation material accumulation, and this condition is named pseudoexfoliation keratopathy.[20(22)] Both pseudoexfoliation keratopathy and the presence of subclinical inflammation might affect wound healing and SIA after a trabeculectomy. Like interleukins and growth factors, inflammatory cytokines promote wound healing and tissue fibrosis.[11] Therefore, some differences between the POAG and XFG cases should exist because of subclinical inflammation and other clinical differences. In our study, we observed significantly higher SIA values in the XFG cases at the first and third postoperative months than in the POAG cases, although the difference was not significant at the sixth month. Significantly higher SIA values within three months might be associated with extended subclinical inflammation in the XFG cases. In addition, changes in corneal biomechanics and corneal hysteresis due to exfoliation may result in this difference. We also observed higher rates of WTR astigmatism in the POAG cases, while higher rates of ATR astigmatism were remarkable in the XFG cases at the sixth month. The XFG cases had shown a greater ATR shift at the sixth month compared to the POAG cases. Other than wound healing, many factors might have affected this result. For example, the presence of exfoliation material and probable zonular laxity might have induced more prominent changes in the anterior segment, and those factors might have affected WTR or ATR astigmatism.

We also observed significant correlations between the SIA and IOP changes in the XFG group at the first and sixth postoperative months, which might be related with a greater IOP decrease in the XFG group. Also, Kim et al.[23] reported that greater SIA was developed in patients with postoperative low intraocular pressure.

In conclusion, a trabeculectomy can decrease IOP significantly and cause SIA due to the changes in the anterior segment parameters related with bleb formation and IOP decrease in POAG and XFG cases. To the best of our knowledge, no previous studies have compared trabeculectomy induced astigmatism in POAG and XFG cases. The increased SIA levels and ATR shift in XFG might be related to the presence of exfoliation material, extended subclinical inflammation, and more prominent changes in the anterior segment in XFG cases. The major limitation of our study is its short duration. Further investigations with a greater number of cases, different types of glaucoma, and longer durations should be encouraged.

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