

Incidence of presumed steroid response in contralateral eye of patients who underwent glaucoma filtration surgery

Rinal Pandit, Ronnie J George, Vijaya Lingam, Shantha Balekudaru

Purpose: The aim of this study was to report the incidence of presumed steroid response in contralateral eye of patients who underwent glaucoma filtration surgery. **Methods:** We reviewed records of 298 glaucoma patients (147 PACG [primary angle-closure glaucoma], 129 POAG [primary open-angle glaucoma], and 22 JOAG [juvenile open-angle glaucoma]) who underwent either trabeculectomy alone or trabeculectomy with cataract extraction. All patients received prednisolone acetate 1% eye drop postoperatively in the operated eye for up to 6 to 8 weeks. The contralateral eye received the same antiglaucoma medications as before. Information collected included age, sex, number of antiglaucoma medications in the fellow eye preoperatively, and VFI (visual field index). The preoperative intraocular pressure (IOP) in the contralateral eye was taken as the baseline. The maximum IOP recorded postoperatively up to a follow-up period of 6 to 8 weeks was noted. A steroid response was defined as rise in the IOP by ≥ 6 mmHg. **Results:** In this study, 298 eyes of 298 glaucoma patients were included. The mean age of patients was 60.1 ± 13.7 years. The mean number of antiglaucoma medications in the fellow eye pre-operatively was 2.4 ± 1.2 . Mean preoperative and postoperative IOP in the fellow eye were 17.46 ± 7 and 19.37 ± 7.1 mmHg, respectively. Sixty-three eyes out of 298 eyes (21.14%) showed a rise in IOP by 6 mmHg. The maximum IOP difference noted was 15 mmHg. The average time interval to the defined steroid response was 16.13 days. The majority showed a steroid response within 19 days. **Conclusion:** Steroid response is a significant factor leading to elevated IOP postoperatively in the contralateral eye as well.

Key words: Fellow eye, glaucoma filtration surgery, IOP, steroid response

Controlling inflammation after glaucoma surgery is of utmost importance for bleb survival, and thus the use of topical steroid forms an important part of postoperative management.^[1] Although steroids reduce postoperative inflammation, they are known to have significant side effects, one of which is elevation of intraocular pressure (IOP).^[2,3] The rise in IOP in the same eye following use of steroids, either topical^[2] or systemic,^[4] has been well-documented. However, the steroid response in fellow eye following the use of steroid in one eye is less well recognized. Consensual ophthalmotonic reaction is the term coined to describe the corresponding pressure changes in the contralateral eye after alteration of IOP in one eye.^[5]

A spectrum of changes can occur in the fellow eye following glaucoma surgery in one eye. A complex set of mechanisms that control the IOP may be involved, including neuronal, hormonal, cytokine, and systemic drug effects.^[6,7] The predominance of a single mechanism resulting due to a particular intervention may guide the IOP changes in the fellow eye. The present study determines the effect of the use of topical steroids in the operated eye over the IOP in the fellow eye.

Methods

Electronic records of 435 consecutive patients with glaucoma who underwent glaucoma filtration surgery either trabeculectomy or phacoemulsification along with trabeculectomy from January 2017 to March 2018 at a tertiary

eye hospital was examined. Patients with primary open-angle glaucoma (POAG), primary angle-closure glaucoma (PACG) and juvenile open-angle glaucoma (JOAG) were included. The nonglaucomatous fellow eyes of unilateral disease were also included. Patients with secondary glaucoma, patients using preoperative systemic antiglaucoma medications, patients who were noncompliant with antiglaucoma medication in the fellow eye at any point of time during the postoperative period were excluded. We included 298 eyes of 298 patients who met the study criteria.

The information collected included age, sex, type of glaucoma, type of surgery (trabeculectomy alone or trabeculectomy combined with phacoemulsification), number of preoperative antiglaucoma medications in the fellow eye, preoperative IOP in the fellow eye measured closest to the surgery, highest IOP in the fellow eye within 6 to 8 weeks of surgery, time interval to the highest IOP in fellow eye, and visual field index (VFI) values of both the eyes wherever applicable.

The same surgical technique was used in all patients undergoing trabeculectomy, including creating a partial thickness scleral flap followed by the application of mitomycin C 0.04% in the subconjunctival space before entry into the eye. For patients undergoing combined surgery, in single-site

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Cite this article as: Pandit R, George RJ, Lingam V, Balekudaru S. Incidence of presumed steroid response in contralateral eye of patients who underwent glaucoma filtration surgery. Indian J Ophthalmol 2021;69:2481-3.

Access this article online

Website:

www.ijo.in

DOI:

10.4103/ijo.IJO_3069_20

Quick Response Code:



Department of Glaucoma, Sankara Nethralaya, Chennai, Tamil Nadu, India

Correspondence to: Dr. Ronnie J George, Sankara Nethralaya (Main Campus), No. 41 (Old 18), College Road, Chennai - 600 006, Tamil Nadu, India. E-mail: drrg@snmail.org

Received: 28-Sep-2020

Revision: 26-Jan-2021

Accepted: 07-Apr-2021

Published: 25-Aug-2021

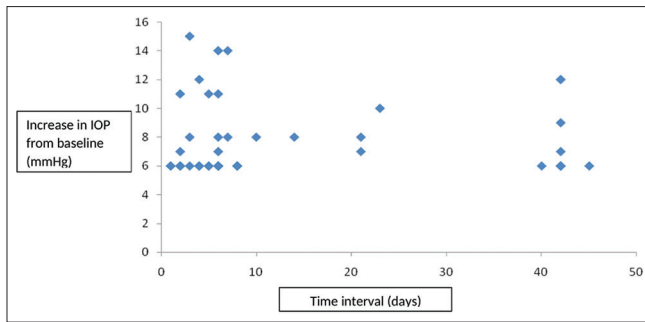


Figure 1: Scatterplot showing relation between the magnitude of steroid response and the number of days within which it was noted

technique, phacoemulsification was done through the same scleral flap fashioned for trabeculectomy and in two-site technique, phacoemulsification was done through a separate temporal clear corneal incision. A foldable acrylic posterior chamber intraocular lens (IOL) implant was used in both groups.

Postoperatively all patients received prednisolone acetate 1% eye drops in the operated eye in a weekly tapering regimen for a minimum of 6 weeks. The preoperative antiglaucoma medication that was used in the operated eye was withheld postoperatively. In the contralateral eye, patients continued the same antiglaucoma medication as was being used preoperatively except for four patients who did not require any antiglaucoma medication for IOP control. Compliance with antiglaucoma medications in the fellow eye was confirmed by directly asking the patient about the usage during each postoperative visit. All patients were examined on Day 1, and the follow-up visits thereafter were variable according to the requirement of trabeculectomy bleb management. All patients were followed up for at least 6 to 8 weeks. All patients underwent IOP measurement in both eyes using Goldmann applanation tonometry during each postoperative visit. The time of IOP measurement was within 2 hours of measurement at each visit. Steroid response in the fellow eye was defined as rise in IOP by ≥ 6 mmHg from the preoperative baseline IOP.^[8] IOP was measured by the same examiner at the baseline and at all time points following surgery. The rise in IOP in the contralateral eye was managed by adding antiglaucoma medication in the same eye as well as considering early and rapid tapering of steroid medication in the operated eye.

Statistical analysis

Data analysis was performed using the IBM SPSS Statistics, Version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were computed for all the variables measured. Chi-square test for independence was used to study the association between the defined steroid response and the diagnostic type of glaucoma.

Results

Two hundred and ninety-eight patients met the inclusion criteria and were included in the study, 188 (63.1%) of them were men and 110 (36.9%) were women. The mean age was 60.11 ± 13.7 years (range = 14–91 years). There was no difference in age between men and women. Table 1 provides the diagnosis details: majority were PACG (147, 49.3%) followed by POAG (129, 43.2%) and JOAG (22, 7.3%).

The mean number of antiglaucoma medications (which includes beta blockers, prostaglandin analogues,

Table 1: Diagnosis of operated eye and fellow eye

Diagnosis	Operated eye (n)	Fellow eye (n)	Age (mean \pm SD)
PACG	147	143	62.38 \pm 10.05
POAG	129	129	62.92 \pm 10.71
JOAG	22	22	28.45 \pm 12.08
Nonglaucomatous fellow eye		4	
Total	298	298	

PACG: Primary angle-closure glaucoma, POAG: primary open-angle glaucoma, JOAG: juvenile open-angle glaucoma

Table 2: Steroid responders and non-responders in each group

Diagnosis	Steroid response (IOP ≥ 6 mmHg from baseline)	No steroid response	Total
PACG	37 (25.17%)	110	147
POAG	20 (15.5%)	109	129
JOAG	6 (27.27%)	16	22
Total	63 (21.14%)	235	298

PACG: Primary angle-closure glaucoma, POAG: primary open-angle glaucoma, JOAG: juvenile open-angle glaucoma

topical carbonic anhydrase inhibitors, pilocarpine, and alpha agonists) being used in the fellow eye preoperatively was 2.4 ± 1.2 . Twelve patients had undergone glaucoma surgery in the fellow eye, and no antiglaucoma medication was being used after surgery. Mean preoperative and postoperative IOP in the fellow eye were 17.46 ± 7 mmHg and 19.37 ± 7.1 mmHg, respectively. Seventy-four (24.8%) patients underwent trabeculectomy alone, and 224 (75.2%) patients underwent trabeculectomy combined with phacoemulsification. Steroid response (rise in IOP ≥ 6 mmHg from the baseline) was noted in 63 eyes out of 298 eyes (21.14%). The maximum IOP difference noted was 15 mmHg. The average time interval to the defined steroid response was 16.13 days. The majority showed a steroid response within 19 days. Persons with JOAG were most likely to present with a steroid response in the fellow eye [Table 2 and Fig. 1]. The maximum number of eyes showing steroid response belonged to the PACG group, but the difference from the POAG group did not reach statistical significance ($P = 0.132 > 0.05$). Mean VFI for responders was $63.39 \pm 36.51\%$, and the mean VFI for the nonresponders was $68.89 \pm 31.51\%$ ($P = 0.384 > 0.05$).

Discussion

In our study, we noted a presumed steroid response of equal or more than 6 mmHg in the contralateral fellow eyes of 21% of the study population, 6 to 8 weeks following surgery.

The existence of a cross-over effect on the fellow eye owing to usage of antiglaucoma medication in one eye has been documented. Timolol is the drug that has been most commonly known to decrease the IOP in the contralateral eye as well. The magnitude of this cross-over effect has been studied by several researchers^[6,9,10] and more than 2.5 mmHg change has not been documented. In the present study, the steroid response has been defined as rise of IOP by ≥ 6 mmHg compared with the baseline. This defined rise is definitely more than what would be expected by just a reversal of the effect of antiglaucoma medication in the operated eye, especially considering the fact

that majority of the glaucomatous fellow eyes was on medical treatment.

Diestelhorst and Kriegelstein^[6] postulated that the filtration surgery in one eye triggers a central nervous system-mediated reflective increase in the aqueous outflow to maintain the physiological stability in the anterior chamber of the surgically treated eye. This central nervous system reflex on the aqueous humor dynamics affects both the eyes and might contribute to the increase in IOP in the fellow eye.

Although the effect produced by the postulated neuronal mechanism cannot be ruled out, it is unlikely to produce the defined rise in IOP alone and might just partly contribute to the obtained rise in IOP.

There have been conflicting reports regarding the IOP changes in the contralateral eye following glaucoma surgery. Vysniauskiene *et al.*^[11] reported a decrease in IOP following surgical reduction in one eye. A *post hoc* analysis of data of the Collaborative Initial Glaucoma Treatment study by Radcliffe *et al.*^[12] demonstrated no substantial effect of trabeculectomy in the fellow eye. In contrast to this, Yarangumeli *et al.*^[13] reported a rise in IOP in the fellow eye following trabeculectomy in one eye.

A prospective interventional study carried out by Kaushik *et al.*^[14] found a significant rise in IOP in both normal and glaucomatous fellow eyes following glaucoma surgery. They found a uniform increase in the fellow eye IOP across all categories of patients, including those with glaucomatous or nonglaucomatous fellow eyes, or those who had received systemic acetazolamide or not as compared with the baseline at all time points up to a follow up of 6 weeks.

None of the above-mentioned studies have attributed the rise in IOP in the fellow eye to one single factor.

Many glaucoma patients require administration of oral acetazolamide for adequate control of IOP prior to surgery. This oral medication, when withdrawn after the surgery, can lead to rise in the IOP in the fellow eye, which might have been masked preoperatively. In our study, this masking effect produced by the use of oral acetazolamide has been eliminated by excluding all the patients who required oral acetazolamide preoperatively.

All the patients were instructed to use the same antiglaucoma medications postoperatively in the fellow eye, and the compliance was confirmed at each visit. The patients who failed to use the antiglaucoma medication at any of the postoperative visit were excluded. Thus, the probability of rise in IOP due to failure of usage of antiglaucoma medication in the fellow eye was ruled out in the present study.

Our study has tried to attribute the rise in IOP obtained in the fellow eye due to a presumed steroid response and has tried to best eliminate the influence of other factors that might additionally contribute to the rise in IOP in the fellow eye.

To the best of our knowledge, there has not been any similar study in the literature that has studied the effect of a single factor leading to rise in IOP in the fellow eye following glaucoma surgery. In many instances, the fellow eye is often the one with useful vision. Also, fellow eyes already damaged by glaucomatous process may be at a significant risk of glaucomatous progression due to higher IOP in the postoperative period. Failure to recognize and monitor IOP changes carefully may unnecessarily delay treatment and appropriate management of these eyes. Thus, fellow eye of all patients undergoing glaucoma filtration surgery requires careful monitoring of IOP during the postoperative period.

The limitations of our study are its retrospective nature, small sample size, and few patients in each diagnostic type of glaucoma that is not enough to conclude whether there exists any statistically significant difference in the steroid response between PAOG, PACG, and JOAG. Also, the influence of factors such as withdrawal of antiglaucoma medication in the operated eye and the possibility of a neuronal mechanism leading to increased aqueous production in the fellow eye cannot be ruled out.

Conclusion

In conclusion, we would like to highlight that steroid response is a significant risk factor for elevated IOP postoperatively in the contralateral eye. One should be cognitive of this fact in managing glaucoma patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Araujo SV, Spaeth GL, Roth SM, Starita RJ. A ten-year follow-up on a prospective, randomized trial of postoperative corticosteroids after trabeculectomy. *Ophthalmology* 1995;102:1753-9.
2. McLean JM. Use of ACTH and cortisone. *Trans Am Ophthalmol Soc* 1950;48:293-6.
3. Bernstein HN, Mills DW, Becker B. Steroid-induced elevation of intraocular pressure. *Arch Ophthalmol* 1963;70:15-8.
4. Weekers L. Modification expérimentales de l'ophtalmotonous. Reaction ophtalmotonique consensuelle. *Arch Ophthalmol (Paris)* 1924;41:641-58.
5. Feher J. *Glaucoma: Pathophysiology of the Eye*. Budapest: Académiai Kiadó Publications; 1998.
6. Diestelhorst M, Kriegelstein G. The effect of trabeculectomy on the aqueous humor flow of the unoperated fellow eye. *Graefes Arch Clin Exp Ophthalmol* 1991;229:274-6.
7. Nuyen B, Weinreb RN, Robbins SL. Steroid induced glaucoma in the pediatric population. *J AAPOS* 2017;21:1-6.
8. Piltz J, Gross R, Shin DH, Beiser JA, Dorr DA, Kass MA, *et al.* Contralateral effect of topical beta-adrenergic antagonists in initial one-eyed trials in the ocular hypertension treatment study. *Am J Ophthalmol* 2000;130:441-53.
9. Zimmerman TJ, Kaufman HE. Timolol: A beta-adrenergic blocking agent for the treatment of glaucoma. *Arch Ophthalmol* 1977;95:601-4.
10. Wilson RP, Kanal N, Spaeth GL. Timolol: Its effectiveness in different types of glaucoma. *Ophthalmology* 1979;86:43-50.
11. Vysniauskiene I, Shaarawy T, Flammer J, Haefliger IO. Intraocular pressure changes in the contralateral eye after trabeculectomy with mitomycin C. *Br J Ophthalmol* 2005;89:809-11.
12. Radcliffe NM, Musch DC, Niziol LM, Liebmann JM, Ritch R; Collaborative Initial Glaucoma Treatment Study Group. The effect of trabeculectomy on intraocular pressure of the untreated fellow eye in the collaborative initial glaucoma treatment study. *Ophthalmology* 2010;117:2055-60.
13. Yarangumeli A, Koz OG, Kural G. The effect of trabeculectomy on the intraocular pressure of the unoperated fellow eye. *J Glaucoma* 2003;12:108-13.
14. Kaushik S, Agarwal A, Kaur S, Lomi N, Raj S, Pandav SS. Change in intraocular pressure in the fellow eye after glaucoma surgery in 1 eye. *J Glaucoma* 2016;25:324-9.