

Effect of Prophylactic Aqueous Suppression on Ahmed Glaucoma Valve Surgery Success

Rini Saha^{1,2}, Riddhi Shah Dharja¹, Graham E. Trope¹, Yvonne M. Buys¹

¹Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada, ²Department of Glaucoma, Iris Superspeciality Eye Hospital, Ranchi, Jharkhand, India

Abstract

Purpose: To evaluate the effect of prophylactic aqueous suppressants immediately post-Ahmed glaucoma valve (AGV) surgery on the rate of hypertensive phase and success.

Methods: Retrospective case-control study of 80 eyes with refractory glaucoma undergoing AGV surgery. Forty eyes in the intervention group (preoperative aqueous suppressants continued postoperatively) and 40 in the control group (all glaucoma drops stopped after surgery and reintroduced as required) were included in this study. Patients were followed for 1 year. Data collected included intraocular pressure (IOP), number of glaucoma medications, and number of eyes requiring further IOP lowering surgery. The frequency of hypertensive phase and 1-year success was compared between the groups.

Results: Hypertensive phase occurred in 22.5% of the intervention group compared to 42.5% of the control group; however, this difference was not statistically significant ($P = 0.06$). Success at 1 year (IOP ≤ 21 mmHg but ≥ 5 mmHg and 20% reduction from baseline without additional surgery) was similar in each group: 77.5% in the intervention group and 62.5% in the control group ($P = 0.22$). However, at 1 year, significantly more eyes in the intervention group had an IOP ≤ 17 mmHg (95% vs. 80%, $P = 0.04$). The mean time interval to a second IOP lowering procedure was significantly shorter in the control group ($P < 0.005$).

Conclusions: With prophylactic preoperative aqueous suppressants, more eyes achieved an IOP of ≤ 17 mmHg. The time interval to repeat the glaucoma procedure was significantly shorter in the control group.

Keywords: Ahmed glaucoma valve, Aqueous suppressants, Hypertensive phase, Intraocular pressure

Address for correspondence: Rini Saha, Iris Superspeciality Eye Hospital, Ranchi - 834 001, Jharkhand, India.

E-mail: rinisaha0706@gmail.com

Submitted: 06-Aug-2021; **Revised:** 03-Mar-2022; **Accepted:** 11-Mar-2022; **Published:** 26-Jul-2022

INTRODUCTION

Glaucoma is a progressive disease of the optic nerve, which may lead to visual field constriction and eventual blindness. Treatment modalities for glaucoma are aimed at lowering intraocular pressure (IOP) and include eye drops, lasers, and surgery.

Glaucoma drainage devices such as the Ahmed glaucoma valve (AGV) gained increasing popularity following publication of the tube versus trabeculectomy (TVT) study which concluded that tube-shunt surgery is an appropriate

surgical option for patients who have undergone prior cataract and/or unsuccessful filtering surgery.¹ In a survey of the American Glaucoma Society members, 57% of respondents indicated that their clinical practice has been significantly impacted by the TVT study and 58.7% that they were more likely to perform tube-shunt surgery instead of a repeat trabeculectomy.²

One of the potential complications of tube-shunt surgery is a hypertensive phase defined as an IOP of >21 mmHg within the first 3–6 postoperative months and has been reported to

Access this article online

Quick Response Code:



Website:
www.jcurrophthalmol.org

DOI:
10.4103/joco.joco_244_21

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

How to cite this article: Saha R, Dharja RS, Trope GE, Buys YM. Effect of prophylactic aqueous suppression on Ahmed glaucoma valve surgery success. J Curr Ophthalmol 2022;34:167-72.

occur in 56%–82% of patients undergoing implantation of AGVs.³ Several studies have shown that the hypertensive phase is most commonly seen with AGVs (40%–80%), in comparison to nonvalved implants.^{3,4} Elevated IOP secondary to the hypertensive phase can result in glaucoma progression and up to 72% of cases elevated IOP may not resolve, signaling early device failure.³

The AGV has a one-way valve which decreases the likelihood of early postoperative hypotony.^{5,6} The subconjunctival space around the plate is exposed to inflammatory mediators and cytokines in the aqueous immediately after surgery and has been proposed as a potential etiology predisposing AGV to the hypertensive phase. Studies on the prevention and treatment of the hypertensive phase have yet to provide a clear consensus on management.⁷ Some studies have evaluated the effect of aqueous suppressants to control the hypertensive phase if the IOP spikes above the target IOP or a predefined range/number.^{8–10}

In 2018, one of the authors (Y.M.B.) altered her post-AGV treatment regimen by continuing aqueous suppressant eye drops postoperatively to potentially decrease the possibility of the hypertensive phase. This retrospective study aims to evaluate the effect of continuing prophylactic aqueous suppressant glaucoma eye drops postoperatively on the rate of hypertensive and success of AGV surgery by comparing the outcome of AGV surgeries pre- and post-2018.

METHODS

This was a retrospective case–control study of patients ≥ 18 years of age with refractory glaucoma who underwent AGV surgery between January 2016 and June 2019 at the glaucoma unit of a tertiary care eye hospital. This study was approved by the University Health Network Research Ethics Board and adhered to the Declaration of Helsinki. Patients allergic to multiple glaucoma eye drops and those with less than 1-year follow-up were excluded from the study. Patient informed consent was taken. The following data were collected from the patients' chart: age at the time of surgery, sex, glaucoma type, operated eye, number of glaucoma surgeries (before and after AGV surgery), IOP (preoperatively and each postoperative visit), number of IOP-lowering medications (preoperatively and each postoperative visit), and complications.

AGV surgery was performed under retrobulbar anesthesia and sedation by a single surgeon (Y.M.B.). All procedures were standardized as follows: a corneal traction suture was placed near the superior limbus. A conjunctival incision was made 6 mm posterior to the limbus in the desired quadrant. After adequate subconjunctival dissection and cautery, two 9-0 prolene sutures were passed through the sclera 8 mm posterior to the limbus and 5 mm apart. The plate of the primed AGV (New World Medical Inc., Rancho Cucamonga, CA, USA) was placed in the subconjunctival pocket and fixed to the sclera using the preplaced prolene sutures.

The anterior chamber was filled with sodium hyaluronate. The AGV tube was trimmed bevel up to the desired length and inserted into the anterior chamber through a corneoscleral tract created using a 22-gauge needle. After satisfactory tube position, a partial thickness corneal graft was placed over the tube. Tenons and the conjunctiva were closed in two layers using 8-0 vicryl.

Postoperative regimen included topical antibiotic drops four times a day for a week and prednisolone acetate every 2 h while awake for 2 weeks, then four times daily for an additional 4 weeks followed by a taper.

For those undergoing surgery after 2018, all preoperative aqueous suppressant eye drops were continued prophylactically, and for those who underwent surgery before 2018, all glaucoma eye drops were stopped after surgery and reintroduced only if required for elevated IOP. Patients were seen on postoperative days 1 and 3, weeks 1, 2, 4, and 6, and months 3, 6, and 12 or more often, if required.

The primary outcomes were to compare the frequency of the hypertensive phase (defined as IOP > 21 mmHg after an initial IOP lowering of ≤ 21 post-AGV surgery in the first 6 months postoperatively) and the success rate. We defined success at 1 year as an IOP of ≤ 21 mmHg but ≥ 5 mmHg and a 20% reduction from baseline without the requirement of a second IOP-lowering procedure. We also calculated success rates using target IOP and various IOP criteria used in other studies of valves^{1,8–11} (IOP ≤ 21 , 17, and 14 mmHg and or 20% reduction from baseline, 30% reduction from baseline without a second IOP lowering-procedure) at 1-year post-AGV. Secondary outcomes included IOP at each visit, number of glaucoma medications, and number of eyes requiring subsequent IOP-lowering procedures.

Data are represented as mean \pm standard deviation and frequency (percentage). Differences between the study groups were compared using the Student's *t*-test or Mann–Whitney *U*-test for continuous variables and Chi-square test or Fisher exact test for categorical variables. All statistical analyses were performed using SPSS version 23 (SPSS Inc., Chicago, IL, USA) with the threshold for statistical significance set at $P < 0.05$. The power of the study based on *post hoc* power analysis using the current sample size is 76.1%.

RESULTS

A total of 80 eyes were included, 40 continuing all preoperative aqueous suppressants immediately postoperatively (intervention group) and 40 receiving aqueous suppressants only as required postoperatively (control group). The mean age was 67.68 ± 14.55 and 68.37 ± 10.68 years in the intervention and control groups, respectively ($P = 0.82$). The demographic characteristics of the study groups are depicted in Table 1. No significant differences were observed between the two groups with regard to patient age, sex, preoperative IOP, number of glaucoma medications, type of glaucoma, and number of previous glaucoma surgeries.

The hypertensive phase occurred in 9 (22.5%) of the intervention group and 17 (42.5%) of the control group; however, this difference was not statistically significant ($P = 0.06$). The mean time from the surgery to the occurrence of hypertensive phase was 6.9 weeks (range, 2–24 weeks) in the intervention group and 5.3 weeks (range, 2–24 weeks) in the control group ($P = 0.54$). Significantly more eyes required escalation of glaucoma medications during follow-up in the control group (35 eyes, 87.5%) compared to the intervention group (26 eyes, 65%, $P = 0.02$).

For IOP and number of glaucoma medications, the groups were compared by both including those eyes requiring a second procedure and carrying forward their IOP/number of medications before the repeat procedure and separately by censoring these eyes. Since there was no statistical difference using either approach the results of censoring, those undergoing repeat glaucoma procedures are presented. The number of eyes included in the analysis at each follow-up after censoring was 40 and 40 at weeks 1, 2, 4, and 6, 40 and 39 at week 12, 40 and 34 at 6 months, and 39 and 30 at 1 year in the intervention and control groups, respectively. In the intervention group, 3 out of 4 eyes required a repeat procedure at 1 year, hence 39 eyes were included for analysis at 1 year. Figure 1 shows IOP at each postsurgical follow-up for the two groups. The IOP was lower in the intervention group compared to the control group at most follow-ups although the values were significant only at 2, 6, and 12 weeks postsurgery. As expected, the number of glaucoma medications was significantly higher in the intervention group compared to the control group at all times [Figure 2].

The success rate at 1 year using different IOP criteria in the two groups is shown in Table 2. Significantly more number of eyes achieved an IOP of ≤ 17 mmHg in the intervention

group compared to the control group ($P = 0.04$). Four (10%) underwent subsequent IOP-lowering surgery in the intervention group (3 AGV, 1 transscleral diode) compared to 10 (25%) in the control group (6 AGV, 4 transscleral diode) but was not statistically insignificant ($P = 0.12$). The mean time interval to the subsequent IOP-lowering surgery was significantly shorter in the control group (18.2 ± 7.4 weeks) compared to the intervention group (45.5 ± 13 weeks, $P < 0.005$).

Table 3 details the postoperative complications in each group. There was no significant difference in postoperative complications between the two groups. None of the conjunctival dehiscences caused any leak, device exposure, or infection.

DISCUSSION

In our study, the hypertensive phase occurred in 22.5% of the intervention group compared to 42.5% of the control group; however, this difference was not statistically significant ($P = 0.06$). The postoperative course of AGV surgery is characterized by an early phase of low-to-normal IOP which can be followed by a hypertensive phase characterized by increased IOP secondary to bleb encapsulation.^{3,4} According to one study, a hypertensive phase can occur in 56%–82% of patients undergoing AGV implantation of which in 72% of cases, the elevated IOP did not resolve, suggesting the hypertensive phase may lead to device failure.³ Although the hypertensive phase is observed more commonly after an AGV, it has been reported with other valves such as the Molteno and Baerveldt devices.⁴ The hypertensive phase can be challenging with the risk of continued optic nerve damage in the setting of uncontrolled IOP in advanced refractory glaucoma.

Table 1: Baseline demographic characteristics of the study groups

Parameter	Intervention group (n=40)	Control group (n=40)	P
Mean age (years)±SD	67.68±14.55	68.30±10.68	0.82
Gender (male, female)	20, 20	16, 24	0.66
Preoperative IOP (mmHg)	20.15±4.93	20.02±6.94	0.93
Mean number of preoperative glaucoma medications±SD	3.75±1.02	3.68±1.29	0.43
Mean number of previous glaucoma surgeries	1.32±0.87	1.19±0.80	0.57
Trabeculectomy	40	36	
AGV	14	8	
Glaucoma type			0.9
Primary open-angle	26	26	
Chronic angle-closure	4	5	
Uveitic	2	2	
Neovascular	2	2	
Juvenile open-angle	3	1	
Pseudoexfoliation	1	2	
Pigmentary	1	1	
Steroid-induced	1	-	
Postkeratoplasty	-	1	

Intervention group: Continuing all preoperative aqueous suppressants immediately postoperatively, Control group: Receiving aqueous suppressants only as required postoperatively. Pearson Chi-square test was used for categorical variables, and Student *t*-test was used for continuous variables in statistical analysis. SD: Standard deviation, IOP: Intraocular pressure, AGV: Ahmed glaucoma valve

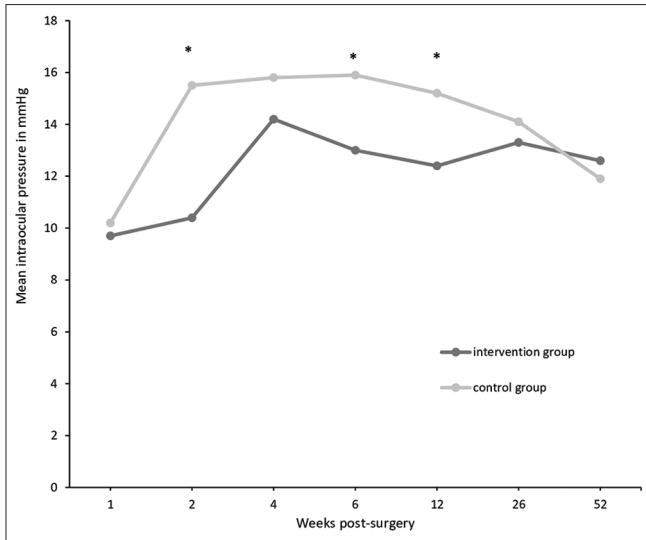


Figure 1: Mean intraocular pressure (IOP) for intervention versus control group over time. The IOP for those eyes that underwent a second IOP-lowering procedure was censored after the procedure. Intervention group – continuing all preoperative aqueous suppressants immediately postoperatively. Control group – receiving aqueous suppressants only as required postoperatively.

Table 2: Success rate at 1 year based on different intraocular pressure criteria

Parameter*	Intervention group, n (%)	Control group, n (%)	P
Achieved target IOP	34 (85)	28 (70)	0.10
IOP≤21 mmHg and 20% reduction	31 (77.5)	25 (62.5)	0.22
IOP≤17 mmHg and 20% reduction	31 (77.5)	24 (60)	0.09
IOP≤14 mmHg and 20% reduction	26 (65)	22 (55)	0.36
IOP≤21 mmHg	39 (97.5)	36 (90)	0.17
IOP≤17 mmHg	38 (95)	32 (80)	0.04
IOP≤14 mmHg	31 (77.5)	25 (62.5)	0.14
20% reduction from baseline	31 (77.5)	27 (67.5)	0.31
30% reduction from baseline	25 (62.5)	24 (60.5)	0.82

*Any eye undergoing a repeat procedure was considered a failure for each of these definitions. Intervention group: Continuing all preoperative aqueous suppressants immediately postoperatively, Control group: Receiving aqueous suppressants only as required postoperatively. Pearson Chi-square test was used for categorical variables in statistical analysis. IOP: Intraocular pressure

Table 3: Summary of postoperative complications

Complication	Intervention group, n (%)	Control group, n (%)
Conjunctival dehiscence	11 (27.5)	9 (22.5)
HypHEMA	11 (27.5)	12 (30)
Aqueous misdirection	1 (2.5)	1 (2.5)

P=0.97. Intervention group: Continuing all preoperative aqueous suppressants immediately postoperatively, Control group: Receiving aqueous suppressants only as required postoperatively

The hypertensive phase occurs due to encapsulation around the plate which is an integral part of the wound healing

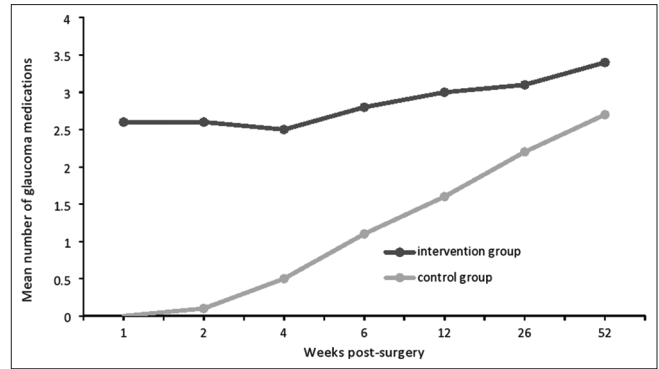


Figure 2: Mean number of glaucoma medications for the intervention group versus the control group over time. Eyes undergoing a second glaucoma procedure were censored after the procedure. Intervention group – continuing all preoperative aqueous suppressants immediately postoperatively. Control group – receiving aqueous suppressants only as required postoperatively

process. Histopathologic analyses of postoperative capsules have shown that by 4 months, the capsules demonstrate thickening and become progressively less cellular, with a layer of fibroblasts replacing macrophages on the inner capsule wall. The capsules reached maximal thickness at 4–6 months when the encapsulating collagen stroma then became less dense.^{12,13} Histopathologic findings suggest that postoperative aqueous flow through the drainage device may contribute to the process of capsule formation. Capsules from surgeries with immediate exposure to aqueous are reportedly thicker compared to capsules resulting from staged procedures with initial tube occlusion and no aqueous drainage in the immediate postoperative period. This has resulted in the hypothesis that either early mechanical force from immediate aqueous drainage and/or immediate exposure to a pro-inflammatory cytokine present in the aqueous humor leads to the hypertensive response. This is consistent with the clinical finding that AVGs have increased rates of hypertensive phase.¹⁴ Owing to the role of inflammatory cytokines in aqueous, early aqueous suppression has been suggested as a method to prevent the hypertensive phase after AGV surgery.

This retrospective comparative study evaluated the effect of continuing aqueous suppressant glaucoma eye drops in the immediate postoperative period following AGV surgery on the rate of hypertensive phase and success. There was a lower frequency of hypertensive phase (22.5% vs. 42.5%, $P=0.06$) in the intervention group compared to the control group, although the difference was not statistically significant. In patients with severe stage glaucoma, high IOP due to the hypertensive phase can cause further damage. The intervention group had a lower mean IOP at most follow-ups with significantly lower IOP at 2, 6, and 12 weeks postsurgery compared to the control group. Hence, prophylactic aqueous suppressant eye drops show slightly better IOP control over the 1st year. Since every mmHg counts, it may be a better way to manage AGVs. Higher IOP can continue optic nerve damage. Law *et al.* randomized patients to initial postoperative glaucoma

medications when IOP reached 10 mmHg (low-IOP initiation group) or 17 mmHg (moderate-IOP initiation group). They reported that eyes with hypotensive therapy started at higher IOPs resulted in higher mean IOPs during the first 2–4 months and continued up to 1 year postoperatively.⁸

We used IOP criteria of IOP ≤ 21 mmHg but ≥ 5 mmHg and a 20% reduction from baseline and no repeat IOP-lowering procedure to define success. In the literature, studies have used varying IOP criteria to define success including ≤ 21 mmHg,^{1,8,10} ≤ 17 mmHg,¹¹ ≤ 14 mmHg,^{9,11} and or 20% reduction from baseline and 30% reduction from baseline.^{1,9,11} Using these various criteria, we found statistically significantly more eyes in the intervention group achieved an IOP ≤ 17 mmHg at 1 year ($P = 0.04$) which is a better IOP for most glaucoma patients. Pakravan *et al.* randomized 94 patients to either receive early aqueous suppression with combination dorzolamide-timolol drops when postoperative IOP became higher than 10 mmHg or to receive normal stepwise treatment when their postoperative IOP exceeded their individualized target pressure. They found that, in patients with early aqueous suppression, there was a significantly higher rate of surgical success in addition to a decreased rate of hypertensive phase (23.4% vs. 66.0% in the conventional treatment group, $P \leq 0.001$). Their results suggest that the early use of aqueous suppressant may result in better outcomes regarding IOP reduction, hypertensive phase frequencies, and success rate.⁹

Another study in rabbit eyes demonstrated that after AGV, early treatment with aqueous suppressants decreased fibrosis of the bleb after glaucoma shunt operation and lowered IOP at 1 month. Prostaglandin analog treatment did not significantly affect collagen deposition in the bleb or postoperative IOP. The authors suggested that when clinically selecting glaucoma eye drops after tube surgery, the effects of glaucoma medication on the wound healing response should be considered.¹⁵ Another study showed better IOP control during the hypertensive phase and a higher surgical success rate after AGV with the use of aqueous suppressants compared to prostaglandin analogs.¹⁰

The need to repeat glaucoma procedure was lower in the intervention group compared to the control group although it was not statistically significant (10% vs. 25%, $P = 0.12$), it can be clinically meaningful, especially from a quality of life standard and financial standard. Noteworthy is that the mean time interval to the subsequent IOP-lowering surgery was significantly shorter in the control group (18.2 ± 7.4 weeks) compared to the intervention group (45.5 ± 13 weeks) with $P < 0.005$. This can again be important from a quality of life standard and financial standard.

In our study, significantly more eyes needed escalation of hypotensive drops at 1-year follow-up in the control group (87.5%) compared to the intervention group (65%, $P = 0.02$) although the mean number of glaucoma medications in the intervention group was significantly more at all-time points. The increased number of glaucoma medications in the intervention group is due to the fact that patients were

continued on all preoperative aqueous suppressant eye drops immediately after postsurgery.

This study has some limitations. This study is retrospective in nature with small sample size. The follow-up period is 1 year only.

To the best of our knowledge, this is the first study evaluating the effect of continuing aqueous suppressant glaucoma eye drops prophylactically immediately following AGV surgery. There was a lower frequency of hypertensive phase and repeat glaucoma procedures by continuing aqueous suppressants prophylactically although the difference was not statistically significant, it can be clinically meaningful. Although there was no significant difference in the number of eyes achieving an IOP ≤ 21 mmHg and a 20% reduction from baseline at 1-year follow-up, significantly more number of eyes achieved an IOP < 17 mmHg which is a better IOP for glaucoma patients. The IOP control also seems to be slightly better in the 1st year after surgery with prophylactic aqueous suppression. The time interval to repeat the procedure was significantly lower in the control group. Prophylactic aqueous suppression might be a better way to manage AGV surgery.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL. Tube versus Trabeculectomy Study Group. Treatment outcomes in the TubeVersusTrabeculectomy (TVT) study after five years of follow-up. *Am J Ophthalmol* 2012;153:789-803.
- Panarelli JF, Banitt MR, Sidoti PA, Budenz DL, Singh K. Clinical impact of 8 prospective, randomized, multicenter glaucoma trials. *J Glaucoma* 2015;24:64-8.
- Nouri-Mahdavi K, Caprioli J. Evaluation of the hypertensive phase after insertion of the Ahmed glaucoma valve. *Am J Ophthalmol* 2003;136:1001-8.
- Ayyala RS, Zurakowski D, Monshizadeh R, Hong CH, Richards D, Layden WE, *et al.* Comparison of double-plate Molteno and Ahmed glaucoma valve in patients with advanced uncontrolled glaucoma. *Ophthalmic Surg Lasers* 2002;33:94-101.
- Francis BA, Cortes A, Chen J, Alvarado JA. Characteristics of glaucoma drainage implants during dynamic and steady-state flow conditions. *Ophthalmology* 1998;105:1708-14.
- Prata JA Jr., Mermoud A, LaBree L, Minckler DS. *In vitro* and *in vivo* flow characteristics of glaucoma drainage implants. *Ophthalmology* 1995;102:894-904.
- Robert A, Fargione RA, Tansuebchueasai N, Lee R, Tania Tai TY. Etiology and management of the hypertensive phase in glaucoma drainage device surgery. *Surv Ophthalmol* 2019;64:217-24.
- Law SK, Kornmann HL, Giaconi JA, Kwong A, Tran E, Caprioli J. Early aqueous suppressant therapy on hypertensive phase following glaucoma drainage device procedure: A randomized prospective trial. *J Glaucoma* 2016;25:248-57.
- Pakravan M, Rad SS, Yazdani S, Ghahari E, Yaseri M. Effect of early treatment with aqueous suppressants on Ahmed glaucoma valve implantation outcomes. *Ophthalmology* 2014;121:1693-8.
- Lee J, Park CK, Jung KI. Initial Glaucoma medication in the hypertensive phase following Ahmed valve implantation: A comparison of results achieved using aqueous suppressants and prostaglandin analogs. *J Clin*

- Med 2020;9:E416.
11. Budenz DL, Barton K, Feuer WJ, Schiffman J, Costa VP, Godfrey DG, *et al.* Ahmed Baerveldt Comparison Study Group. Treatment outcomes in the Ahmed Baerveldt Comparison Study after 1 year of follow-up. *Ophthalmology* 2011;118:443-52.
 12. Lloyd MA, Baerveldt G, Nguyen QH, Minckler DS. Long-term histologic studies of the Baerveldt implant in a rabbit model. *J Glaucoma* 1996;5:334-9.
 13. Molteno AC, Fucik M, Dempster AG, Bevin TH. Otago glaucoma surgery outcome study: Factors controlling capsule fibrosis around Molteno implants with histopathological correlation. *Ophthalmology* 2003;110:2198-206.
 14. Freedman J, Iserovich P. Pro-inflammatory cytokines in glaucomatous aqueous and encysted Molteno implant blebs and their relationship to pressure. *Invest Ophthalmol Vis Sci* 2013;54:4851-5.
 15. Jung KI, Woo JE, Park CK. Effects of aqueous suppressants and prostaglandin analogues on early wound healing after glaucoma implant surgery. *Sci Rep* 2019;9:5251.