Simultaneous Ahmed Glaucoma Valve Implantation with Intravitreal and Intracameral Bevacizumab in Refractory Acute Stage of Neovascular Glaucoma: Short-Term Results and Complications

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Abstract

***Purpose*:** To examine the safety and efficacy of simultaneous Ahmed glaucoma valve (AGV) implantation with intravitreal and intracameral injection of bevacizumab (IVB and ICB) in patients with refractory acute neovascular glaucoma (NVG) with very high intraocular pressure (IOP) and active neovascularization of the iris (NVI) and/or the angle (NVA)

***Methods*:** In a prospective interventional study, patients presenting with acute NVG with uncontrolled IOP despite maximally tolerated medical treatment and with no prior history of interventions for their ischemic retinal condition underwent AGV implantation and IVB and ICB injection. Their baseline clinical data including the etiology of NVG, visual acuity (VA), IOP and the number of anti-glaucoma medications were recorded. Postoperatively, VA, IOP and number of anti-glaucoma medications and any complications were recorded. The main outcome measure was IOP control with and without medical therapy.

***Results*:** Six eyes of 6 patients were recruited in the study. All of them had diabetic NVG. The mean age of the patients was 62.6±7.8 years. Mean IOP and number of medications were 61.5±9.9 mmHg and 4.1±.4, respectively. Three months after the surgery, the mean IOP and the number of medications were 19.5±4.5 mmHg and 2±1.26, respectively. The most frequent complication was hyphema (occurring in all eyes) that resolved spontaneously during the first postoperative week in 5 eyes and necessitated anterior chamber (AC) washout in 1 eye. Postoperatively, two eyes developed choroidal effusions and shallow ACs which resolved without any intervention during the first postoperative month.

***Conclusion*:** In patients with acute NVG with no prior treatment whose IOP was very high despite maximal medical therapy, AGV implantation with simultaneous IVB and ICB injection effectively reduced IOP and medications use in short-term. The most frequent complication was development of hyphema (in all eyes) which spontaneously resolved in most eyes.

***Keywords*:** Neovascular Glaucoma, Bevacizumab, Ahmed Glaucoma Valve

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Introduction

Neovascular glaucoma (NVG) is a type of secondary glaucoma which has been associated with a poor prognosis.[1] NVG is believed to result from retinal ischemia that induces production of vasoproliferative factors such as vascular endothelial growth factor (VEGF). VEGF causes neovascularization of the anterior segment on the iris (NVI) and anterior chamber angle (NVA), which can lead to refractory angle closure glaucoma. NVG often presents acutely with pain, redness, and blurred vision and elevated intraocular pressure (IOP).[2]

The management of NVG has two aspects: IOP control either medically or surgically, and treatment of the underlying retinal disease.[3]

Usually medical treatment is started first to control IOP and inflammation. Complete panretinal photocoagulation (PRP) is performed as soon as practicable.[3] After these measures, if IOP is not controlled glaucoma surgery is usually indicated.

Recently intravitreal bevacizumab (IVB) has been used in the management of NVG.[5-11] More recently intracameral bevacizumab (ICB) is also introduced in the management of NVG with promising results.[12-14] However, the effect of IVB/ICB is temporary. Usually it is common practice to inject bevacizumab and wait for a time, so neovascularization and inflammation of the anterior segment subside and later surgery (if indicated) can be done with lower risk of intraoperative and postoperative complications.[4]

In the acute stage of NVG, IOP can increase to very high levels. If medical treatment fails, and IOP remains high the chance for permanent optic nerve damage is probable. In this situation there is little time to wait. Lowering IOP promptly in these eyes gives us the time for more definitive treatments of this condition such as PRP. On the other hand, glaucoma surgery in these eyes is associated with high complication profile.

In this study, we report our experience on the short-term results and complications of Ahmed glaucoma valve (AGV) implantation combined with intravitreal and intracameral bevacizumab injection in 6 patients with uncontrolled acute NVG. These patients had no prior treatment for their ischemic retina and no previous surgery for IOP control.

Methods

The study was carried out with approval from the local Ethics Committee, and the study adhered to the tenets of the Declaration of Helsinki. Informed consents were obtained from all patients before surgery.

Six patients in the acute stage of NVG with poor IOP control despite maximally tolerated IOP lowering medical therapy were included in the study. These patients had not been treated with PRP or IVB for their retinal ischemic disorder previously.

All of the eyes underwent AGV implantation (model FP-7, New World Medical Inc.) in the superotemoporal quadrant. The procedure was performed under local anesthesia. A superior corneal traction with 7-0 polyglactin or 7-0 silk suture was placed, and the globe was rotated inferiorly. A conjuctival incision was performed 4-5 mm posterior to the limbus, and a limbus-based conjunctiva and Tenon's fascia flap was dissected. The plate of the AGV was fixated to the sclera with two 8-0 nylon sutures 8-10 mm posterior to the limbus. In phakic eyes the tube was inserted into the anterior chamber (AC) from a sclerostomy that was made with a 23G needle 1 millimeter posterior to the limbus. In pseudophakic eyes, an inferotemporal limabal stab was made with 15-degree knife and viscoelastic was injected behind the iris to inflate the sulcus space in the superotemporal quadrant. Then the tube was inserted into the sulcus through a 23 gauge sclerostomy 1-2 mm posterior to limbus. Scleral or corneal patch graft was placed over the episcleral portion of the tube and fixed to the sclera with 8-0 polygalactin suture. Tenon's fascia and conjunctiva were sutured with 8-0 polyglactin running sutures. In 3 phakic eyes tube was inserted into the AC and in the other 3 pseudophakic eyes tube was inserted into the ciliary sulcus. Figure 1 shows the tube in ciliary sulcus of patient number 6 at 3 months follow-up visit. At the end of the procedure 1.25 mg per 0.05 ml bevacizumab (Avastin; Genentech Inc.) was injected intravitreally in the inferotemporal quadrant, 3-4 millimeter posterior to limbus with a 27G needle and 1.25 mg per 0.05 ml of bevacizumab was also injected in AC.

Preoperative data were recorded in the patients' charts and included age, sex, visual acuity (VA), intraocular pressure measured by

Goldmann applanation tonometry and glaucoma medications. Postoperatively, all patients were referred to the retina service for further treatment of their retinal ischemic conditions. For this report the data of the first 3 postoperative months of patients are presented. In all postoperative visits VA measurement and slit-lamp examination were performed, and IOP and number of glaucoma medications and also complications were recorded. Surgical success was defined as: 6 mmHg≤IOP≤21 mmHg and ≥20% reduction in baseline IOP (with or without anti-glaucoma medications) at the last follow-up visit without loss of LP vision.

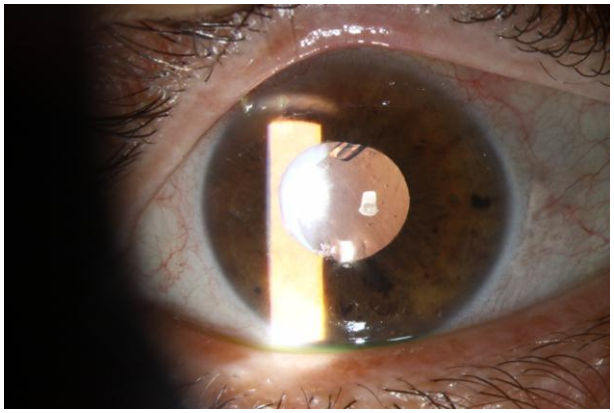

Figure 1. Postoperative slit-lamp photograph of the tube of Ahmed glaucoma valve within the ciliary sulcus of the patient number 6

Results

Six patients with refractory acute NVG underwent simultaneous AGV implantation and intravitreal and intracameral bevacizumab injection. In all of these patients, NVG was secondary to diabetic retinopathy. Table 1 summarizes the preoperative and postoperative data regarding the baseline and postoperative visits of the patients. Mean age of the patients was 62.6±7.8 years. Figure 2 shows the mean IOP of the study eyes pre- and postoperatively. Mean baseline IOP decreased from 61.5±9.9 mmHg to 19.5±4.5 mmHg at 3 months postoperatively (68% decrease in IOP). Mean number of glaucoma medications decreased from 4.1±.4 preoperatively to 2±1.26 at 3 months postoperatively. According to our study criteria in 5 of 6 eyes the procedure were considered successful.

At 3 months follow-up visit, VA improved in 3 eyes, in 2 eyes no change occurred in VA and in 1 eye VA decreased from hand motion (HM) to light perception (LP); patient 5.

Intraoperative hyphema developed in all of the eyes. Postoperatively the hyphema resolved in all cases during a week except in patient number 5. In this patient the hyphema did not decrease and clogged the tube and IOP increased; therefore AC washing was done for her on 7th day after the surgery.

Postoperatively two of the patients (case 5 and 6) developed choroidal effusions and shallow AC which resolved spontaneously without any intervention during the first month after surgery. In one eye (patient number 6) conjunctival erosion over the patch graft was noted 6 weeks postoperatively. The patient refused to be operated for this complication, so we placed her on autologous serum eye drops every 4 hours and preservative-free steroid eye drop bid and topical chloramphenicol eye drop tid. Three months after surgery the scleral patch graft was partially melted, but conjunctival epithelialization and vascularization was seen over the tube.

Table 1. Preoperative and postoperative data regarding the patients and eyes undergoing the surgery

Case number	Age	sex	Pre-op			2 weeks post-op			6 weeks post-op			3 months post-op		
			VA	IOP	Med	VA	IOP	med	VA	IOP	Med	VA	IOP	Med
1	49	M	LP	70	4	0.1	18	-	0.1	28	-	0.1	15	3
2	60	F	HM	55	5	0.1	14	-	0.3	15	-	0.4	20	-
3	69	M	.1	45	4	0.4	14	-	0.4	23	2	0.4	18	2
4	62	M	.1	62	4	FC 3m	6	-	0.1	12	-	0.1	19	1
5	65	F	HM	67	4	LP	14	-	LP	25	-	LP	28	3
6	71	F	LP	70	4	LP	6	-	HM	32	1	LP	17	3

VA: Visual acuity, IOP: Intraocular pressure, Med: Glaucoma medications, Pre-op: Preoperative, Post-op: Postoperative

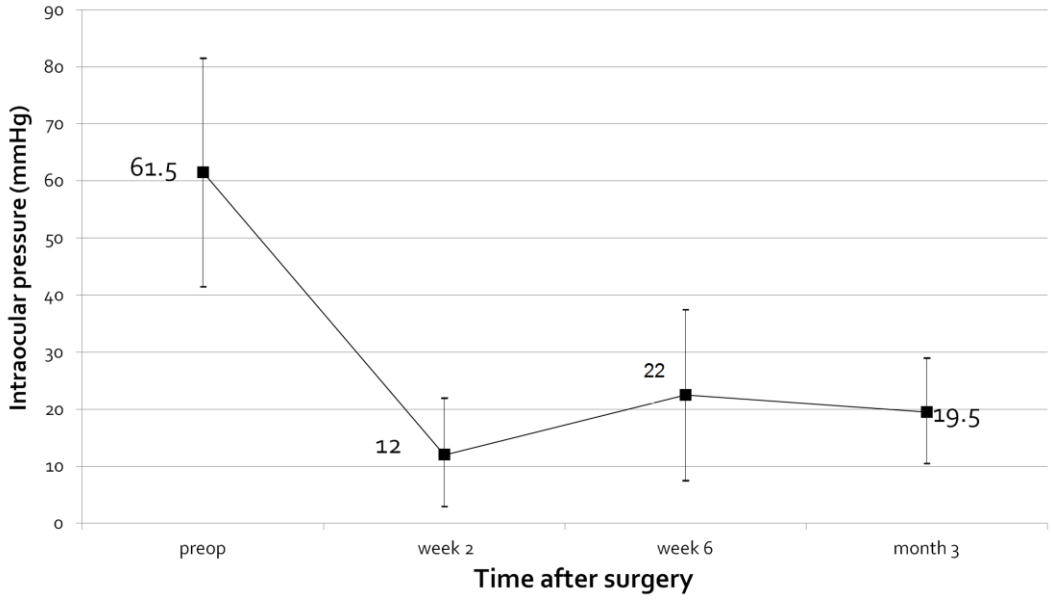

Figure 2. Intraocular pressure before and after surgery

Discussion

In this study we reported on 6 cases of acute NVG with very high IOP levels despite maximal medical therapy. In these patients, an urgent lowering of IOP was needed. Therefore, we decided to perform AGV implantation combined with intracameral and intravitreal injection of bevacizumab. Our results showed that this procedure effectively reduced IOP in short-term although the complication rate was high. Our work is noteworthy in that we reported on patients with very high levels of IOP (mean: 61.5 mmHg; range: 45-70 mmHg), with active NVI/NVA in the acute phase of NVG and with no prior intravitreal injection or laser or surgical procedures.

NVG is one of the most difficult types of glaucoma to treat. Without appropriate treatment, it usually has an aggressive course which leads to blindness.[1] Ischemic retina, the most common cause of NVG, releases VEGF, which in turn stimulates new vessel growth on the iris surface and the AC angle. This fibrovascular membrane occludes the trabecular meshwork and causes open angle glaucoma. In later stages this membrane contracts and the resultant peripheral anterior synechiae (PAS) formation causes angle closure glaucoma.[1,3]

Intravitreal injection of bevacizumab has been shown to cause the regression of AC new vessels in NVG.[4-6] This modality has been used for IOP control in these eyes either alone or as an adjuvant with other treatments such as trabeculectomy, cyclodestructive procedures, or glaucoma drainage device implantation.[6-10] Its effects as a sole treatment of NVG are not long lasting and the majority of the patients will eventually need some other treatments.[4,11,12]

Recently, intracameral injection of bevacizumab was reported to effectively reduce the high levels of VEGF in the AC of eye with NVG.[13] Furthermore, ICB is shown to decrease the permeability of the new vessels and cause them to regress rapidly.[14] Wolf et al, found that in the treatment of NVG ,ICB lowered IOP for about 3 weeks and they proposed ICB as a means for IOP control until more definitive treatments for NVG are performed.[15]

Glaucoma drainage devices have long been used for IOP control in NVG with variable degrees of success rates.[10,16,17] Their success seems to be lower in NVG than other types of glaucoma.[18] It has been shown that higher VEGF levels in aqueous humor of NVG patients is associated with higher failure rate of AGV implantation,[19] therefore it has been suggested that anti-VEGF agents could be used prior to AGV implantation in these eyes.[10]

In some patients with acute NVG and highly elevated IOP refractory to medical

treatment an urgent glaucoma surgery is needed. Because of the critical situations of our patients, we decided to use AGV combined with IVB and ICB for IOP control, in order to be able to save the eye, and give the eye more time before PRP can be performed. Short-term results of this procedure were favorable. Corneal edema had resolved in all of them during the first week, which allowed us to visualize the posterior segment and to perform PRP.

In this study the tube of AGV was inserted in the AC in 3 phakic eyes, and the tube was inserted in the ciliary sulcus in the other 3 pseudophakic eyes. Ciliary sulcus placement of the tubes can decrease the potential of corneal endothelial decompensation in pseudophakic or aphakic eyes.[20,21] In a recent study by Hau et al, decreased corneal endothelial cell density after tube insertion in AC was significantly associated with the degree of preoperative PAS.[22] Patients with NVG usually have some degrees of PAS, so AC placement of tubes can be associated with greater risk to corneal endothelium, so ciliary sulcus insertion of tubes may be advantageous in these patients.

The most prevalent complication was hyphema which was higher than other studies.[18,23] The reason may be that we performed surgery in the acute stage of NVG with active NVA/NVA, so the rate of hyphema in our patients would be higher. The other major complication was choroidal effusion and shallow AC (in two) which resolved with no intervention.

The major limitation of this report is the small number of cases and short follow-up time. A study with more patients and longer follow-up period will reveal a more detailed and stronger evidence of outcome of this procedure in acute NVG patients.

Conclusion

In summary, this study showed that in patients with acute stage NVG with no prior treatment whose IOP was very high despite maximal medical therapy, AGV implantation with simultaneous intravitreal and intracameral bevacizumab is effective in controlling the IOP in short-term. Although hyphema occurred in all eyes, in most eyes it was self-limited and resolved during 1 week after surgery.

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