# A Pilot Study Assessing Treatment Outcomes in Neovascular Glaucoma Using Ahmed Glaucoma Valve with and without Cyclophotocoagulation

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# **A**BSTRACT

**Purpose:** The purpose of this retrospective pilot study was to examine the short-term effect of simultaneous Ahmed Glaucoma Valve implantation and cyclophotocoagulation on postoperative outcomes in patients with neovascular glaucoma.

Methods and materials: Patient charts were selected for inclusion in this study if they carried a diagnosis of neovascular glaucoma and underwent Ahmed glaucoma valve implantation only, Ahmed glaucoma valve implantation with cyclophotocoagulation, or cyclophotocoagulation only. A total of 55 eyes of 54 patients were selected for data collection and analysis. Main outcome measures included 1-, 3-, and 6-month intraocular pressure and occurrence of the hypertensive phase. Other outcomes included visual acuity, surgical complication rate, and a number of 6-month postoperative ophthalmic medications.

Results: A significantly lower intraocular pressure was seen in the group that received Ahmed glaucoma valve implantation + cyclophotocoagulation compared to the Ahmed glaucoma valve-only group at 3 and 6 months (p = 0.03 and <0.001, respectively). The difference in the occurrence of the hypertensive phase between the Ahmed glaucoma valve-only group and the Ahmed glaucoma valve + cyclophotocoagulation group approached but did not reach significance (p = 0.052). A significantly lower intraocular pressure was also seen in the cyclophotocoagulation-only group compared to the Ahmed glaucoma valve-only group at 3 months (p = 0.006).

**Conclusion:** Simultaneous Ahmed glaucoma valve implantation and cyclophotocoagulation significantly lowered intraocular pressure at 3 and 6 months compared to Ahmed glaucoma valve implantation alone in patients with neovascular glaucoma.

Clinical significance: Neovascular glaucoma is difficult to manage medically and surgically. When surgery is performed, intraocular pressure often remains elevated postoperatively despite aggressive medical management. This study examines a novel method to lower intraocular pressure after Ahmed glaucoma valve implantation in patients with neovascular glaucoma.

**Keywords:** Ahmed glaucoma valve, Cyclophotocoagulation, Hypertensive phase, Intraocular pressure, Neovascular glaucoma, Retrospective pilot cohort study.

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# Introduction

Neovascular glaucoma (NVG) is a particularly aggressive form of glaucoma that is difficult to manage medically and surgically. In the advanced stages of NVG, surgical interventions are indicated to reduce intraocular pressure (IOP). Multiple surgical interventions are available to reduce IOP in NVG, but no single modality of treatment has been identified as being superior and most do not afford long-term success. Both glaucoma drainage devices (GDD) and cyclophotocoagulation (CPC) have been shown to be efficacious in lowering IOP in patients with NVG, although with modest abiding favorable outcomes. 2

The Ahmed Glaucoma Valve (AGV, New World Medical Inc, Cucamonga, CA) is an implantable device that shunts aqueous fluid from the anterior chamber (AC) to the subconjunctival space. The AGV is intrinsically designed to minimize postoperative hypotony.<sup>3</sup> One complication associated with the AGV is the hypertensive phase (HP), which is characterized by an increase in IOP >21 mm Hg within the first 6 months following surgery, after a successful reduction of IOP to <22 mm Hg during the first postoperative week. This IOP increase is also not caused by tube obstruction, retraction, or valve malfunction.<sup>4-8</sup>

The etiology of the HP has not yet been fully determined. One of the proposed mechanisms involves the timing and amount of aqueous fluid exposure to the bleb surrounding the GDD. In AGV

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implantation, there is early aqueous flow into the bleb surrounding the device. This early aqueous exposure can produce characteristic histological changes in the bleb capsule. These changes result in a thicker and/or less permeable capsule, which can impair the drainage capacity of the device and yield the increased IOP seen in the HP. Inflammatory cytokines (such as TGF $\beta$ -2, IL-6, IL-10, and CXCL1) present in the aqueous fluid may serve as a molecular impetus for the histologic changes seen in the HP. However, it

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remains unclear whether these cytokines play a causal role in the development of the HP or are merely a reaction to the high IOP during the HP.

A study by Pakravan et al.,<sup>7</sup> and a separate study by Law et al.,<sup>8</sup> found that early medical aqueous suppressant therapy reduced the incidence of the HP in AGV drainage devices. These studies suggest that reducing aqueous fluid production in the early postoperative course may reduce the incidence of the postoperative IOP elevation associated with the HP. Although early aqueous suppression helps improve outcomes after AGV implantation, NVG remains difficult to manage and poor outcomes are often seen despite aggressive postoperative management.<sup>1</sup>

CPC reduces aqueous humor production by using a laser to ablate the ciliary body. CPC has been used as a primary treatment for glaucoma as well as a treatment for glaucoma refractory to medical and surgical management.<sup>13,14</sup> Few studies have explored the simultaneous use of CPC and GDDs to manage glaucoma.<sup>15,16</sup> The authors of this study are not aware of any study to date that has investigated CPC as an adjuvant therapy to AGV implantation in patients with NVG. The aim of this study is to determine whether simultaneous CPC and AGV implantation improve postoperative outcomes in NGV patients.

# MATERIALS AND METHODS

# **Study Population**

This retrospective pilot study consisted of 55 eyes from 54 patients with NVG who underwent AGV implantation alone, CPC alone or, combined AGV and CPC from December 2015 through November 2019. This study adhered to the tenants of the Declaration of Helsinki and Institutional Review Board (IRB)/Ethics Committee approval was obtained at the University of North Carolina-Chapel Hill. All patients in the study received their eye care at the University of North Carolina Kittner Eye Center. All surgeries were performed by three eye surgeons (D.F., M.R.K., or O.J.K) or by fellows under their supervision. Patients were excluded if they were under 18 years of age, had less than 1 month of follow-up, or received a prior AGV implant within 6 months of the surgery analyzed in this study.

### **Data Collection**

Patients were screened by ICD-10 and CPT codes associated with neovascular glaucoma and the surgeries involved in the study, respectively. Demographic and clinical data, including age, gender, ethnicity, race, NVG risk factors, medical diagnoses, prior glaucoma surgery, preoperative and 6-month postoperative lens status, preoperative ophthalmic medications, preoperative visual acuity, operative eye, duration of steroid use, and frequency of steroid use were recorded from patient charts that met the criteria for the study. CPC settings and the number and location of applied shots were recorded. All applications of CPC used the trans-scleral approach. The main outcome measures were IOP at 1 month, 3 months, and 6 months postoperatively and the presence of a hypertensive phase. There was insufficient data available to make a comparison between groups at time points greater than 6 months. The hypertensive phase was defined as an IOP > 21 mm Hg within the first 6 months following surgery, after a successful reduction of IOP to <22 mm Hg during the first postoperative week, and unrelated to tube obstruction, retraction, or valve malfunction. Additional outcome measures were 6-month ophthalmic medications, 1-, 3-, and 6-month visual acuity, and surgical complications. One-day and 1-week postoperative IOP was also collected. Visual acuity was converted from a Snellen equivalent to a LogMAR value.

Postoperative time points of 1 month, 3 months, and 6 months were selected for data collection to assess the progression of postoperative IOP. Due to the fact that not every patient follow-up would fall exactly on the postoperative day specified for this study's data collection, three-time frames were created: postoperative weeks (POWs) 2-8, POWs 9-16, and POWs 17-30. Each of these time frames contained the 1-month, 3-month, and 6-month time point. If the follow up was not exactly on the 1-month, 3-month, or 6-month postoperative date, the date of follow-up within each time frame that was closest to the 1-month, 3-month or 6-month time point was selected for data analysis. If two points were equidistant from one another, the follow-up that was furthest in distance from the operative date was selected. The majority of postoperative follow-ups (80 out of 131) were within 10 days of the intended postoperative follow-up date. If a follow-up was more than 10 days away from the intended postoperative follow-up date, researchers marked this data point and recorded the amount of days between the actual follow-up visit and the intended follow-up date.

### Intraocular Pressure Measurement

Tools used to measure IOP included Goldmann Applanation Tonometer, Tonopen, and Icare. In some follow-ups, IOP was measured multiple times. In certain situations, a patient's IOP was elevated, and IOP measurements were taken before and after IOP lowering agents were administered. In these situations, the reading taken before the medical intervention was used. If multiple readings were taken without medical intervention between measurements, the reading from the Goldmann Applanation Tonometer was used. If readings using the Goldmann Applanation Tonometer were not taken, readings using the Tonopen or Icare were used, with priority given to the Tonopen reading if both were available. If multiple IOP readings in the context of one follow-up visit were taken from the same device without medical intervention between the readings, the recorded IOP was an average of the available readings.

### **Statistical Analysis**

A total of 30 patients met the criteria for analysis who received only an AGV implant. A total of 13 patients were identified who received an AGV implant and CPC. A total of 12 patients met the criteria for analysis who received CPC only. The Student's *t*-test was used to compare quantitative variables between two groups. Either Pearson's Chi-squared test or Fisher's exact test was used to comparing qualitative variables between groups. An ANOVA with a Bonferroni *post hoc* correction was used to compare data involving more than two groups. For variables involving repeated measures within individual subjects (IOP, visual acuity, and ophthalmic medications), an ANOVA that utilized a generalized estimating equation was used to account for multiple observations within subjects. The Kruskal-Wallis nonparametric test was used to analyze data on steroid duration, dose, and frequency. All data was analyzed using the SPSS Statistics software version 26 (IBM, Armonk, NY).

## RESULTS

### **Patient Demographics**

This retrospective pilot study consisted of 55 eyes from 54 patients with neovascular glaucoma. The Ahmed-only group consisted of

30 eyes, the Ahmed + CPC group consisted of 13 eyes, and the CPC-only group consisted of 12 eyes. The three groups did not differ significantly by age, gender, race, ethnicity, NVG risk factors, medical diagnoses, accompanying surgical procedure, or surgical eye. The CPC-only group had significantly more patients with prior AGV surgery. The demographic data for the three groups is displayed in Table 1.

# **Surgical Complications**

There was no significant difference in surgical complication rate between the three groups. The most common surgical complication was a HP, occurring in 21 eyes (70%) in the Ahmed-only group and 5 eyes (38.5%) in the Ahmed + CPC group. The difference incidence of a HP between the Ahmed-only and Ahmed + CPC approached, but did not reach, significance with a p of 0.052. In the Ahmed-only group, hyphema occurred in five eyes (16.7%), choroidal effusion occurred in two eyes (6.7%), malignant glaucoma occurred in two eyes (6.7%), tube obstruction occurred in one eye (3.3%), uveal effusion occurred in one eye (3.3%), and suprachoroidal hemorrhage occurred in one eye (3.3%). In the Ahmed + CPC group, hyphema occurred in two eyes (15.4%), and tube obstruction occurred in three eyes (23.1%). The CPC-only group had one eye (8.3%) experience postoperative hypotony. Both the Ahmed-only and Ahmed + CPC group each had one eye (3.3 % and 7.7%, respectively) convert to no light perception (NLP). The CPC group did not have any eyes convert to NLP. The surgical complication data is displayed in Table 2.

### **Intraocular Pressure**

The preoperative IOP was 39.1  $\pm$  10.7 mm Hg for the Ahmed-only group, 49.0  $\pm$  20.0 mm Hg for the Ahmed + CPC group, and 40.6  $\pm$  13.89 mm Hg for the CPC-only group. There was no significant difference in the preoperative IOPs between the groups (p > 0.05). There was a significantly lower IOP at the 3-month time point in the Ahmed + CPC group compared to the Ahmed-only group (p = 0.03). The CPC-only group also showed a significantly lower IOP at the 3-month time point compared to the Ahmed group (p = 0.006). At the 6-month postoperative time point, the Ahmed + CPC group had a significantly lower IOP compared to the Ahmed-only group (p < 0.001). The IOP at all postoperative time points and comparison between time points are displayed in Tables 3 and 4, and Figure 1.

### **Visual Acuity**

The preoperative visual acuity was significantly worse for the CPC-only group with a LogMAR score of 2.45  $\pm$  0.58 compared to Ahmed-only and Ahmed + CPC which had LogMAR scores of 1.75  $\pm$  0.84 and 1.68  $\pm$  0.89, respectively (p = 0.001 and p = 0.007, respectively). This finding was similar at the 1-, 3-, and 6-month time points. The 1-month LogMAR was significantly worse in the CPC-only group compared to the Ahmed + CPC group (p = 0.023). The 1-month and 3-month LogMAR was significantly worse in the CPC-only group compared to the Ahmed-only group (p < 0.001 and p = 0.002, respectively). The 6-month LogMAR was significantly worse in the CPC-only group compared to both the Ahmed-only and Ahmed + CPC groups (p = 0.002 and p = 0.024, respectively). There was no significant difference in visual acuity between the Ahmed-only and Ahmed + CPC groups either preoperatively or at any time postoperatively. The average visual acuity within each group decreased from the preoperative time point compared to the 6-month postoperative time point. The visual acuity data is shown in Table 5.

# **Steroid Usage**

There was no significant difference in the mean duration, number of applications, or applications per day between the three groups. The mean number of days on postoperative ophthalmic steroid drops was 87.1  $\pm$  58.0 for the Ahmed-only group,  $101\pm51.4$  for the Ahmed + CPC group, and 71.1  $\pm$  30.1 for the CPC-only group (p=0.323). The mean number of applications of postoperative ophthalmic steroid drops was 319  $\pm$  211 for the Ahmed-only group, 372  $\pm$  243 for the Ahmed + CPC group, and 238  $\pm$  115 for the CPC-only group (p=0.267). The mean number of applications per day of postoperative ophthalmic steroid drops was 3.75  $\pm$  1.02 for the Ahmed-only group, 3.43  $\pm$  0.91 for the Ahmed + CPC group, and 3.33  $\pm$  0.72 for the CPC-only group (p=0.487).

## **Ophthalmic Medications**

The mean number of preoperative ophthalmic medications was 2.93  $\pm$  0.96 for the Ahmed-only group, 2.23  $\pm$  1.64 for the Ahmed + CPC group, and 2.18  $\pm$  1.25 for the CPC-only group. There was no significant difference in the number of preoperative ophthalmic medications between any of the groups (p > 0.05). The mean number of 6-month postoperative ophthalmic medications was 1.75  $\pm$  0.91 for the Ahmed-only group, 1.43  $\pm$  0.98 for the Ahmed + CPC group, and 1.13  $\pm$  1.13 for the CPC-only group. There was no significant difference in the number of 6-month ophthalmic medications between the three groups (p > 0.05).

### **Phakic Status**

Preoperatively, 53.3% of the Ahmed-only group, 46.2% of the Ahmed + CPC group, and 58.3% of the CPC-only group were phakic, while the remaining percentage in each group was pseudophakic. At the 6-month postoperative time point, 43.3% of the Ahmed-only group, 30.7% of the Ahmed + CPC group, and 41.7% of the CPC-only group were phakic, while the remaining percentage in each group was pseudophakic. There was no significant difference in the preoperative or 6-month postoperative phakic status between the three groups (p=0.827 and p=0.603, respectively).

# **Quadrants of CPC Treatment**

The mean number of quadrants of CPC treatment was 2  $\pm$  0.57 in the Ahmed + CPC group and 2.82  $\pm$  0.41 in the CPC-only group (p < 0.001). The settings of CPC treatment also varied between the two groups. The Ahmed + CPC group settings ranged from 1250–1500 mW, and each patient received 4 seconds of treatment. The CPC-only settings ranged from 1250–2700 mW, and duration of treatment ranged between 2 and 4 seconds.

### Discussion

This study was the first to examine the use of CPC as an adjuvant to AGV implantation in patients with NVG. NVG is regarded as one of the most difficult types of glaucoma to treat, given that it is often unresponsive to treatment and can require significant intervention to manage. The use of the AGV to treat NVG is associated with a variety of complications, with the HP being one of the most prevalent. The etiology of the HP after GGD still remains unclear. It has been shown that the AGV is more prone to bleb encapsulation and HP than other GGD. 17,18 Ayyala et al. 17 showed that the AGV had a higher incidence of the HP compared to the Double Plate



 Table 1: Demographic, medical, and surgical characteristics of study population

	Total	Ahmed	Ahmed + CPC	CPC	<b>p</b> comparison of study groups
Sample size	n = 55	n = 30	n = 13	n = 12	
Age, mean ± SD	54.0 ± 12.9	53.6 ± 12.2	52.7 ± 12.7	55.8 ± 10.9	0.805 <sup>a</sup>
Gender, number (%)					
Male	27 (49.1)	17 (56.7)	6 (46.2)	4 (33.3)	0.328 <sup>b</sup>
Female	28 (50.9)	13 (33.3)	7 (53.8)	8 (66.7)	
Ethnicity, number (%)					
Hispanic	15 (27.3)	7 (23.3)	4 (30.7)	4 (33.3)	0.764 <sup>c</sup>
Not-Hispanic	40 (72.7)	23 (76.7)	9 (69.2)	8 (66.7)	
Race, number (%)					
African American	26 (47.3)	16 (53.3)	5 (38.5)	5 (41.7)	0.834 <sup>c</sup>
Caucasian	12 (21.8)	6 (20)	4 (30.7)	2 (16.7	
Other	15 (27.3)	7 (23.3)	4 (30.7)	4 (33.3)	
Asian	2 (3.6)	1 (3.3)	0 (0)	1 (8.3)	
NVG risk factor, number (%)	•	•	• •	-	
PDR	46 (83.6)	23 (76.7)	13 (100)	10 (83.3)	0.165 <sup>c</sup>
CRVO	2 (3.6)	2 (6.7)	0 (0)	0 (0)	0.421 <sup>c</sup>
CRAO	3 (5.5)	2 (6.7)	0 (0)	1 (8.3)	0.589 <sup>c</sup>
CRVO/CRAO (Combine Mechanism)	2 (3.6)	2 (6.7)	0 (0)	0 (0)	0.421 <sup>c</sup>
CRVO/BRAO (Combine Mechanism)	1 (1.8)	1 (3.3)	0 (0)	0 (0)	0.654 <sup>c</sup>
Retinal detachment	1 (1.8)	0 (0)	0 (0)	1 (8.3)	0.161 <sup>c</sup>
Medical diagnosis, number (%)					
T2DM	47 (85.5)	24 (80)	12 (92.3)	11 (91.7)	0.453 <sup>c</sup>
T1DM	7 (12.7)	5 (16.7)	1 (7.7)	1 (8.3)	0.630 <sup>c</sup>
HTN	41 (74.5)	21 (70)	11 (84.6)	9 (75)	0.600 <sup>c</sup>
HLD	17 (30.9)	9 (30)	4 (30.7)	4 (33.3)	0.948 <sup>b</sup>
CAD	5 (9.1)	3 (10.0)	1 (7.7)	1 (8.3)	0.966 <sup>c</sup>
CKD	18 (32.7)	8 (26.7)	5 (38.5)	5 (41.7)	0.568 <sup>b</sup>
Carotid-cavernous sinus fistula	1 (1.8)	1 (3.3)	0 (0)	0 (0)	0.654 <sup>c</sup>
Accompanying procedure, number (%)					
Cataract surgery	6 (10.9)	3 (10)	2 (15.4)	1 (8.3)	0.829 <sup>c</sup>
Avastin injection	4 (7.3)	2 (6.7)	1 (7.7)	1 (8.3)	0.980 <sup>c</sup>
Chlorpromazine Injection	1 (1.8)	0 (0)	0 (0)	1 (8.3)	0.161 <sup>c</sup>
AC Chamber Washout	1 (1.8)	1 (3.3)	0	0 (0)	0.654 <sup>c</sup>
Prior AGV implant, number (%)	17 (12.7)	1 (3.3)	0 (0)	6 (50)	<0.001 <sup>cd</sup>
Surgical eye, number (%)					
OD	22 (40.0)	12 (40)	4 (30.7)	6 (50)	0.618 <sup>b</sup>
OS	33 (60.0)	18 (60)	9 (69.2)	6 (50)	

<sup>&</sup>lt;sup>a</sup>Student t-test; <sup>b</sup>Pearson's Chi-squared test; <sup>c</sup>Fisher's exact test; <sup>d</sup>Significant p value; PDR, proliferative diabetic retinopathy; CRVO, central retinal vein occlusion; CRAO, central retinal artery occlusion; T2DM, type 2 diabetes mellitus; T1DM, type 1 diabetes mellitus; HTN, hypertension; HLD, hyperlipidemia; CAD, coronary artery disease; CKD, chronic kidney disease

Molteno device (Molteno Ophthalmic Ltd, Dunedin, New Zealand), and Tsai et al. <sup>18</sup> demonstrated that the AGV had higher rates of bleb encapsulation compared to Baerveldt valves. It has been hypothesized that because there is immediate aqueous fluid exposure to the tissues surrounding the device in AGV implantation, histologic changes occur that cause the encapsulating bleb to become congested, leading to the increase in IOP associated with the HP. <sup>5,11</sup> Molteno et al. <sup>11</sup> demonstrated that in the Molteno

implant, immediate aqueous flow to the tissue surrounding the implant resulted in a thicker bleb capsule. Although no studies have been conducted to examine the histology of bleb capsules in human eyes following AGV implant, it is reasonable to assume that a similar underlying mechanism exists. Further supporting this theory, Pakravan et al. <sup>7</sup> and Law et al. <sup>8</sup> showed that early aqueous fluid suppression may reduce the incidence of the hypertensive phase in AGV implantation. Given the findings of the studies by

Table 2: Surgical complication rate

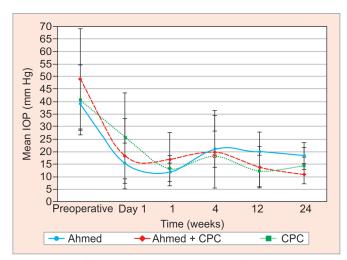
	Total	Ahmed	Ahmed + CPC	CPC	p comparison of study groups
	(n = 55)	(n = 30)	(n = 13)	(n = 12)	
Surgical complication, number (%)					
Hypertensive phase	24 (72.7)	21 (70)	5 (38.5)		0.052 <sup>b</sup>
Hyphema	7 (21.2)	5 (16.7)	2 (15.4)		1 <sup>c</sup>
Choroidal effusion	2 (6.1)	2 (6.7)	0 (0)		1 <sup>c</sup>
Malignant glaucoma	2 (6.1)	2 (6.7)	0 (0)		1 <sup>c</sup>
Tube obstruction	1 (3.0)	1 (3.3)	3 (23.1)		0.075 <sup>b</sup>
Conversion to NLP	2 (3.6)	1 (3.3)	1 (7.7)	0 (0)	0.585 <sup>b</sup>
Uveal effusion	1 (3.0)	1 (3.3)	0		1 <sup>c</sup>
Suprachoroidal hemorrhage	1 (3.0)	1 (3.3)	0		1 <sup>c</sup>
Hypotony	1 (8.3)	0 (0)	0 (0)	1 (8.3)	1 <sup>c</sup>

<sup>&</sup>lt;sup>b</sup>Pearson's Chi-squared test; <sup>c</sup>Fisher's exact test; NLP, No light perception

Table 3: Intraocular pressure at postoperative time points

	Ahmed	n	Ahmed + CPC	n	CPC	n
Preoperative IOP, mean ± SD	39.1 ± 10.7	30	49.0 ± 20.0	13	40.6 ± 13.9	12
1-day IOP, mean, ± SD	$15.3 \pm 8.00$	29	$18.3 \pm 13.0$	12	25.7 ± 17.8	7
1-week IOP, mean ± SD	$11.9 \pm 3.67$	16	$17.0 \pm 10.5$	11	$13.25 \pm 5.25$	4
1-month IOP, mean ± SD	$21.0 \pm 7.2$	30	$20.0 \pm 14.5$	13	$18.2 \pm 18.6$	10
3-month IOP, mean ± SD	$20.0 \pm 7.8$	24	$13.8 \pm 8.30$	11	$12.3 \pm 6.3$	6
6-month IOP, mean $\pm$ SD	$18.3 \pm 5.48$	21	$11.0 \pm 4.34$	8	$14.5 \pm 7.2$	8

IOP, intraocular pressure; SD, standard deviation



**Fig. 1:** Intraocular pressure at preoperative and postoperative time points ranging from 1 day to 24 weeks, in neovascular glaucoma patients who received Ahmed glaucoma valve only, Ahmed glaucoma valve and cyclophotocoagulation, or cyclophotocoagulation only. The error bars represent 1 sd. a superscript d indicates a significant difference from the Ahmed-only group

Pakravan and Law, the study authors routinely treat all post-tube surgery patients with early aqueous suppression. However, medical aqueous suppression alone is often not sufficient at lowering the IOP postoperatively in patients with NVG. The aim of this retrospective pilot study was to demonstrate that using CPC as an

adjuvant to AGV implant could improve postoperative outcomes by reducing aqueous fluid production in the postoperative period.

The authors were able to demonstrate significantly lower IOP at the 3- and 6-month postoperative time points in the AGV + CPC group compared to the AGV-only group. Six-month ophthalmic medications and steroid use between the Ahmed-only and the Ahmed + CPC group did not significantly differ, indicating that CPC likely played a role in lowering the IOP at these time points. In the present study, a significant difference was not observed in the Ahmed group versus the Ahmed + CPC group at 1 week or 1 month. indicating that the maximal reduction in pressure associated with adjuvant CPC was delayed. There is some precedent for this finding. Yildirim et al.<sup>2</sup> found, in a study comparing treatment outcomes with CPC vs AGV implant in patients with NVG, that at the 1-month time point, patients who received CPC had significantly higher IOP than those who received AGV. However, the CPC settings in the Yildirim study had a 2-second application duration with a starting laser power of 1500 mW, which was different from the CPC settings used in the Ahmed + CPC group in the present study. It is worth noting that the CPC group also had its maximal IOP reduction at the 3-6 months time points.

In the present study, the difference in the HP between the Ahmed-only group and the Ahmed + CPC group approached, but did not reach, statistical significance (p=0.052). Given that the IOP lowering benefits of adjuvant CPC were not seen until 3 and 6 months, and the HP can present from postoperative week 1 through postoperative week 24, the adjuvant CPC may have only helped to prevent the HP later in the postoperative course. No other



Table 4: Comparison of intraocular pressure between study groups at postoperative time points

	Preoperative	1 day	1 week	1 month	3 month	6 month
Ahmed vs Ahmed + CPC	0.079	0.433	0.105	0.802	0.03 <sup>d</sup>	<0.001 <sup>d</sup>
Ahmed + CPC vs CPC	0.051	0.304	0.32	0.79	0.657	0.207
Ahmed vs CPC	0.726	0.103	0.582	0.621	0.006 <sup>d</sup>	0.147

<sup>&</sup>lt;sup>d</sup>Significant p value; The statistical test used for comparison was an ANOVA with a generalized estimating equation

Table 5: Visual acuity measured by LogMAR equivalent score at postoperative time points

	Ahmed	Ahmed + CPC	CPC
Preoperative LogMAR, mean $\pm$ SD	$1.75 \pm 0.84$	1.68 ± 0.89	2.45 ± 0.58
1-month LogMAR, mean $\pm$ SD	$1.62 \pm 0.83$	$1.77 \pm 1.00$	$2.45 \pm 0.43$
3-month LogMAR, mean $\pm$ SD	$1.55 \pm 0.94$	$1.66 \pm 1.10$	$2.31 \pm 0.42$
$6$ -month LogMAR, mean $\pm$ SD	$1.57 \pm 0.88$	$1.52 \pm 0.98$	$2.33 \pm 0.50$

SD, standard deviation

significant differences were seen in complication rates between the Ahmed-only group and the Ahmed + CPC group.

The CPC-only group had similar outcomes to the Ahmed + CPC group when compared to the Ahmed-only group. Significant lowering of IOP was seen at 3 and 6 months, but not at 1 week or 1 month. The 1-month IOP of the CPC-only group was lower than what other studies have found. <sup>2,19</sup> This finding could be due to the fact that 68.4% of the CPC-only group had a prior AGV implant. Ness et al. <sup>20</sup> found that in patients with refractory glaucoma who received trans-scleral CPC after a tube shunt failure, the 1-month IOP was approximately 16 mm Hg, which is more consistent with the present study's findings in the CPC-only group. However, the Ness study was not specific to NVG or the AGV implant.

The preoperative visual acuity for the CPC-only group was significantly worse than the Ahmed-only group and the Ahmed + CPC group, which can be explained by the fact that 6 patients in this group underwent CPC for a blind, painful eye, and the rest had failure of their AGV. Of the 12 patients included in the CPC-only group, only one postoperative complication (hypotony) was observed. There is evidence to suggest that a lower rate of complications is seen in CPC compared to GDD.<sup>21</sup>

### Limitations

The limitations of this study include the retrospective nature of data collection. Although the data suggest that adjuvant CPC can improve outcomes in AGV implantation, a randomized controlled trial would be needed to more definitively gauge if this treatment modality is beneficial. The small sample size of this study inherently leads to a lower power and thus a higher probability of a type II error. This small sample size could have diminished the study's ability to detect statistically significant differences that are potentially present in the population of patients with NVG who received these procedures but were not present in this study sample. Ideally, a sample size and power calculation would have been helpful in controlling for a type II error. However, the number of patients who fulfilled the study criteria was very small, especially for the Ahmed + CPC group and CPC-only group. Additionally, combining AGV implantation and CPC has not been studied before in human eyes so a sample size calculation would have been speculation. Given that this is a pilot study of a new surgical method, a main goal was to provide adequate data and a sufficient justification on which to base a prospective study.

Each NVG patient is unique in regard to the extend and location of neovascularization in their eye. For example, some have just neovascularization of the iris, while others may have more extensive neovascularization that involves the optic disk. Due to the small sample size and retrospective nature of this study, the authors included a wide range of clinical presentations of NVG, which potentially presents a confounding variable. Additionally, because each NVG case is unique, the CPC settings were tailored for each patient. This study includes patients who received differing durations and energy settings of CPC. These differing CPC settings likely present an additional confound.

The difference in CPC settings between the Ahmed + CPC group and the CPC-only group, the number of quadrants treated, and the number of prior glaucoma surgeries between the CPC-only group and the two other groups all present likely potential confounders. The six patients in the CPC-only group who received a prior AGV implant received CPC because the implant had failed. We can be reasonably confident that given the greater than six month duration between AGV implantation and CPC, as well as high preoperative IOP (indicating device failure), that these patient's Ahmed valves were nonfunctional. The authors' inclusion of the CPC-only group was to provide a level of comparison for patients who had NVG but did not receive simultaneous AGV implantation and CPC. The authors recognize that interpretation of the data comparing the two groups who received CPC should be done with caution, but given the nature of the study design, the authors believe this comparison provided useful information.

This study highlights the potential for combined AGV implant and CPC in patients with NVG. Significantly lower IOP was seen at designated postoperative time points in the Ahmed + CPC group compared to Ahmed-only group. No significant difference in IOP at any postoperative time point was observed between the Ahmed + CPC group and the CPC-only group. However, the CPC-only group had substantial confounders that made comparison with this group limited. This study provides the justification for a larger, prospective study to examine the long term outcomes of combined AGV implantation and CPC.

# CONCLUSION

While this study has limitations, most notably its retrospective nature and small sample size, the authors conclude that simultaneous CPC and AGV implantation appears to lower IOP in the 3–6 months postoperative time frame compared to AGV implantation alone in patients with NVG. Surgeons should consider this approach to prevent an IOP spike within the 3–6 months postoperative time frame in patients with NVG who received AGV implantation. However, further randomized control trials are needed to more fully understand the benefits of combined CPC and AGV implantation in patients with NVG.

# CLINICAL SIGNIFICANCE

NVG is a difficult disease to manage. Even after NVG patients receive surgical intervention, the IOP often remains elevated despite the addition of aqueous suppressant therapy. This study examined a novel method for lowering IOP postoperatively in patients with NVG who receive the AGV implant. It was demonstrated that combined AGV implantation and CPC is an effective method for lowering the IOP in patients with NVG in the short-term. This study also provides the basis for a larger, prospective study in the future.

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### REFERENCES

- Shchomak Z, Sousa DC, Leal I, et al. Surgical treatment of neovascular glaucoma: a systematic review and meta-analysis. Graefes Arch Clin Exp Ophthalmol 2019;257(6):1079–1089. DOI: 10.1007/s00417-019-04256-8
- Yildirim N, Yalvac IS, Sahin A, et al. A comparative study between diode laser cyclophotocoagulation and the Ahmed Glaucoma Valve implant in neovascular glaucoma. J Glaucoma 2009;18(3):192–196. DOI: 10.1097/IJG.0b013e31817d235c
- 3. Coleman AL, Hill R, Wilson MR, et al. Initial clinical experience with the Ahmed glaucoma valve implant. Am J Ophthalmol 1995;120(1):23–31. DOI: 10.1016/s0002-9394(14)73755-9
- Won HJ, Sung KR. Hypertensive phase following silicone plate Ahmed glaucoma valve implantation. J Glaucoma 2016;25(4):e313 – e317. DOI: 10.1097/IJG.0000000000000249
- Nouri-Mahdavi K, Caprioli J. Evaluation of the hypertensive phase after insertion of the Ahmed glaucoma valve. Am J Ophthalmol 2003;136(6):1001–1008. DOI: 10.1016/s0002-9394(03)00630-5
- Ayyala RS, Zurakowski D, Smith JA, et al. A clinical study of the Ahmed glaucoma valve implant in advanced glaucoma. Ophthalmology 1998;105(10):1968–1976. DOI: 10.1016/S0161-6420(98)91049-1
- Pakravan M, Rad SS, Yazdani S, et al. Effect of early treatment with aqueous suppressants on Ahmed glaucoma valve implantation outcomes. Ophthalmology 2014;121(9):1693–1698. DOI: 10.1016/j. ophtha.2014.03.014

- Law SK, Kornmann HL, Giaconi JA, et al. Early aqueous suppressant therapy on hypertensive phase following glaucoma drainage device procedure. J Glaucoma 2016;25(3):248–257. DOI: 10.1097/IJG.000000000000131
- 9. Faragione RA, Tansuebchueasai N, Lee R, et al. Etiology and management of the hypertensive phase in glaucoma drainage-device surgery. Surv Ophthalmol 2018;64((2019)):217–224. DOI: 10.1016/j. survophthal.2018.10.008
- Jung KI, Park H, Jung Y et al. Serial changes in the bleb wall after glaucoma drainage implant surgery: characteristics during the hypertensive phase. Acta Ophthalmol 2015;93(4):248–253 DOI: 10.1111/aos.12571
- Molteno AC, Fucik M, Dempster AG, et al. Otago glaucoma surgery outcome study: factors controlling capsule fibrosis around Molteno implants with histopathological correlation. Ophthalmology 2003;110(11):2198-2206 DOI: 10.1016/S0161-6420(03)00803-0
- 12. 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(7):4851–4855. DOI: 10.1167/iovs.13-12274
- Canadanovic V, Tusek-Ljesevic L, Miljkovic A, et al. Effect of diode laser cyclophotocoagulation in treatment of patients with refractory glaucoma. Vojnosanit Pregl 2015;72(1):16–20. DOI: 10.2298/vsp1501016c
- Shields MB. Diode laser transscleral cyclophotocoagulation as a primary surgical treatment for primary open-angle glaucoma. Evidence-Based Eye Care 2001;2(4):238–239. DOI: 10.1097/00132578-200110000-00026
- 15. Sapienza JS, Woerdt AVD. Combined transscleral diode laser cyclophotocoagulation and Ahmed gonioimplantation in dogs with primary glaucoma: 51 cases (1996–2004). Vet Ophthalmol 2005;8(2):121–127. DOI: 10.1111/j.1463-5224.2005.00356.x
- Shields SR, Chen P. Sequential or simultaneous cyclophotocoagulation and glaucoma drainage implant for refractory glaucoma. J Glaucoma 2002;11(3):203–208. DOI: 10.1097/00061198-200206000-00007
- Ayyala RS, Zurakowski D, Monshizadeh R, et al. Comparison of double-plate Molteno and Ahmed glaucoma valve in patients with advanced uncontrolled glaucoma. Ophthalmic Surg Lasers 2002;33(2):94–101.
- 18. Tsai JC, Johnson CC, Dietrich MS. The Ahmed shunt versus the Baerveldt shunt for refractory glaucoma: a single surgeon comparison of outcome. Ophthalmology 2003;110(9):1814–1821. DOI: 10.1016/S0161-6420(03)00574-8
- Freigassner P, Eckhardt M. Transscleral cyclophotocoagulation versus cyclocryotherapy in treatment of neovascular glaucoma: a retrospective analysis. Acta Ophthalmol Scand 2003;81(6):674–675. DOI: 10.1111/j.1395-3907.2003.00187.x
- 20. Ness PJ, Khaimi MA, Feldman RM, et al. Intermediate term safety and efficacy of transscleral cyclophotocoagulation after tube shunt failure. J Glaucoma 2012;21(2):83–88. DOI: 10.1097/IJG.0b013e31820bd1ce
- 21. Wang MY, Patel K, Blieden LS, et al. Comparison of efficacy and complications of cyclophotocoagulation and second glaucoma drainage device after initial glaucoma drainage device failure. J Glaucoma 2017;26(11):1010–1018. DOI: 10.1097/ IJG.0000000000000766

