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Original Article

Clinical Challenges with Neovascular Glaucoma-Patient Tailored Strategies and Outcomes

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Abstract

Background: To report the outcomes of patient-tailored concurrent combined surgery for retinal ischemia and intraocular pressure (IOP) control in neovascular glaucoma (NVG) with or without cataract.

Methodology: Patients with Ninety-seven (97) eyes with NVG seen between January 2022-September 2023 at a tertiary eye care centre were recruited for this study. Six (6) eyes (4 proliferative diabetic retinopathy and 2 retinal vein occlusions) that underwent concurrent retinal and glaucoma procedures with or without cataract surgery, were selected. Outcomes after surgery were judged based on the World Glaucoma Association guidelines on reporting glaucoma surgical trials, comprising functional and surgical parameters.

Results: The IOP reduced by>50% from baseline in all 6 eyes, with one eye developing shallow AC by overstraining and 3 eyes developing transient self-resolving hyphema. Two eyes received additional bevacizumab (n=1) or ranibizumab (n=1) injections for persistent DME at 4 and 5 months after surgery. The final IOP was reduced in all eyes at the final follow-up of 6±1.2 months, with one eye requiring 2 medications for IOP control.

Conclusion: The outcomes after concurrent retinal and glaucoma filtering surgery in NVG may be comparable to those of the traditional stepwise approach to management, provided these are offered on a case-by-case basis.

Keywords: Neovascular Glaucoma; Retinal Ischemia; IOP; VEGF; Surgical Outcomes.

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Quick Response Code:

Introduction

Neovascular glaucoma (NVG) comprises a challenging entity associated with a high rate of visual morbidity and blindness if not treated promptly [1,2]. The prognosis depends on the severity and the extent of the underlying pathology, the extent of damage to the optic nerve, and the timely control of intraocular pressure (IOP). Co-existing ocular morbidities, if any, affect the overall outcome and the timely management of this grave condition [1-4]. Early detection and intervention are crucial for better outcomes in NVG, especially those associated with proliferative diabetic retinopathy (PDR), or retinal vein occlusions (RVO). Surgical management of the intraocular pressure and control of retinal ischemia are key for salvaging useful vision in these patients and this calls for a combined strategy addressing IOP control and retinal ischemia in unison [2,3,5-7]. In patients with neovascular glaucoma and coexisting cataracts, successful and timely management of IOP and the underlying ischemia is more challenging owing to poor visibility of the retinal pathology.

Traditionally, anti-VEGF injections are given first to help in the regression of new vessels in the iris/angle followed by glaucoma filtering surgeries for IOP [2,5,7]. In developing countries, this stepwise approach to the management of NVG may be difficult owing to delayed presentations, binocular disease with poor vision in the other eye, high possibility of loss of follow-up after primary interventions, co-existing morbidities like cataracts, inaccessibility to health access centers, and financial constraints of any intervention or the need for frequent reviews [6]. In such special situations, a combination of surgical interventions/procedures for IOP control and retinal ischemia may be required to ensure maximal attempts to salvage useful vision. Adjuvant anti-vascular Endothelial Growth Factor (VEGF), either intravitreal or intracameral, with trabeculectomy with antifibrotics, is reported to improve surgical success and IOP outcomes in NVG. Yet, no study has evaluated the outcomes of combined concurrent retinal interventions and glaucoma surgery, in NVG in patients with delayed presentations and coexisting systemic conditions like cataracts. This series sheds light on the difficulties faced while addressing specific clinical scenarios in NVG, with or without cataracts, and uncontrolled IOP, necessitating a combination of various interventions addressing retinal ischemia and IOP control for the best possible outcomes.

Methodology:

A retrospective chart review was done to identify old or new patients with neovascular glaucoma (due to diabetic retinopathy, DR, or RVO), and uncontrolled IOP on anti-glaucoma medications, with or without previous (>/= 2 months before presentation) retinal laser treatment, intravitreal injection, or other interventions. Those patients who underwent concurrent surgical intervention for glaucoma, retinal interventions for correcting underlying retinal ischemia (intravitreal bevacizumab, anterior retinal cryoablation, or intraoperative retinal photocoagulation), with or without cataract surgery, between January 2022-September 2023 at a tertiary eye care centre in east India, were included in the study. This study was part of a retrospective study evaluating clinical outcomes of primary versus secondary glaucoma which followed the tenets of the Declaration of Helsinki and was approved by the institutional review board of a tertiary eye centre in East India (2014-IM-3). Patients with NVG due to other causes like tumors, ocular ischemic syndrome, trauma, uveitis, and chronic retinal detachment, a follow-up period of less than 3 months, patients with no /perception of light, and patients undergoing isolated glaucoma or retinal procedures, were excluded from the study.

Data retrieved from the hospital electronic medical records database included visual acuity, gonioscopy findings, previous interventions, medication history (at presentation and final follow-up), IOP (at diagnosis, 1 week, 1 month, 3 months or later), duration between diagnosis of primary condition (DR or RVO) to detection of NVG, type of intervention undertaken, and the need for additional medication, surgical or laser intervention (for IOP control and retinal intervention) after the combined procedure.

Outcomes after surgery were judged based on the World Glaucoma Association guidelines on the reporting of glaucoma surgical trials with success being defined if the IOP was less or equal to the target IOP with (qualified) or without (complete) glaucoma medications. Stata Corp (version 13, USA) was used for all statistical analyses including paired student t-test, and Wilcoxon sign rank test, with $p<0.05$ defining statistical significance.

Results:

Of ninety-seven (97) eyes with NVG seen during the period, we identified 6 eyes that underwent concurrent retinal and glaucoma procedures with or without cataract surgery during the stated period. This included 4 eyes with bilateral PDR and NVG and 2 eyes with CRVO, Table 1, Figures 1 and 2. One patient was diagnosed with irido-corneal-endothelial (ICE) syndrome and developed proliferative diabetic retinopathy (PDR) with NVG after 3 years of regular review for IOP, Figure 2. Of these 6 patients, only 2 patients had vision better than 20/40 in the other eye with hypertensive retinopathy, while 2 patients were blind in the other eye at presentation. Table 1.

Table 1: Clinical profile of patients with neovascular glaucoma in special situations with or without cataracts

Age (years)/Gender	Diagnosis in the operated eye	BIOP (mm Hg)	Other eye diagnosis	Reason for a combined strategy	Procedures are done.
50/F	PDR S/p VR surgery and endolaser	55	PDR	Cataract/ Media opacity	PC+IOL+AGV+Bevacizumab
57/M	PDR	37	Absolute NVG	Cataract/ Media opacity -From a different state	AGV+ARC+PC+IOL
51/F	CRVO	34	HTR	Cataract/ Media opacity	PT+IOL+Ranibizumab
61/M	PDR	59	PDR/NVG/absolute	Cataract/ Media opacity Other state	PC+AGV+IOL+Bevacizumab
54/F	PDR with ICE syndrome	30	ICE syndrome	Cataract/ Media opacity	PT with MMC+IOL+Bevacizumab
61/M	CRVO	37	PDR	Different state	Trabeculectomy with MMC + Bevacizumab

AGV-Ahmed glaucoma Valve (FP7, USA); PDR-proliferative diabetic retinopathy; PT-Phacoemulsification with trabeculectomy; PC-phacoemulsification; MMC-mitomycin-C; CRVO-central retinal vein occlusion; ARC-anterior retinal cryopexy; IOL-intraocular lens.

All six patients were on 2-5anti-glaucoma medications at presentation with a mean IOP of 42±10.1mm Hg and 3 patients were on tabs acetazolamide (carbonic anhydrase inhibitor) at presentation. Five patients had previously received anti-VEGF injections or laser pan-retinal photocoagulation (PRP) while 1 patient had no history of prior retinal intervention.

The mean duration of prior retinal intervention in 5 eyes was 3±1.4months with 3 patients having previously received complete PRP sessions at other facilities before presentation at our Center. Five patients underwent concurrent AGV (n=3) or trabeculectomy (n=3) with anti-VEGF (n=5) or anterior retinal cryopexy (ARC) in one eye. Intraoperative bleed was seen in 3 cases which was minimal in nature. Postoperative hyphema less than 1/3rd anterior chamber (AC) was seen in 2 eyes with one eye with ICE syndrome having shallow AC on day 1.

The IOP was reduced in all 6 eyes at 1 week and 1month after surgery with surgical success criteria met in all eyes at final follow-up. Postoperatively, 5 eyes had an additional PRP at 1-2months after surgery. Table 2. Only three patients had transient hyphema (minimal-to 1/3rd chamber) that did not require any additional intervention. Two eyes received additional bevacizumab (n=1) or ranibizumab (n=1) injections for persistent DME at 4 and 5months after surgery, respectively. Figure 2, Table 2. One eye developed a shallow AC with no leak post-Ahmed glaucoma valve surgery which mandated AC reformation, Figure 1, Table 2. The final VA improved to 20/60 in this case with no need for further retinal or glaucoma intervention. The final IOP was reduced in all eyes at the final follow-up of 6±1.2 months, with one eye requiring 2medications for IOP control.

Table 2: Post-operative outcomes after combined surgeries for retinal ischemia and intraocular pressure control in neovascular glaucoma.

Age/Gender	Preop BCVA	IOP at final follow-up	complications	Additional interventions	Time of additional intervention from surgery	Final BCVA
50/F	20/800	12	1day Hyphema<1/3rd AC	Bevacizumab injection	7 days	20/400
57/M	FCCF	10	Flat AC at 3 weeks	AC reformation PRP 3 sittings and FFA-guided add-on laser	8 days	20/60
51/F	FCCF	8	None	Add-on laser PRP	16 days	20/400
61/M	HMCF	16	Trace hyphema on day 1	Multiple laser PRP-4 sittings	6 days	20/250
54/F	20/250	10	Shallow AC at 1day	Add-on Laser PRP-2 sittings	10 days	20/160
61/M	FC1m	20	Trace hyphema on day 1	Bevacizumab injection for macular edema, Laser PRP at	14 days	20/200

FC-Finger counting, FCCF- Finger counting close to face; HMCF-hand movements close to face; BCVA; Best corrected visual acuity; AC-anterior chamber; PRP-pan-retinal photocoagulation.

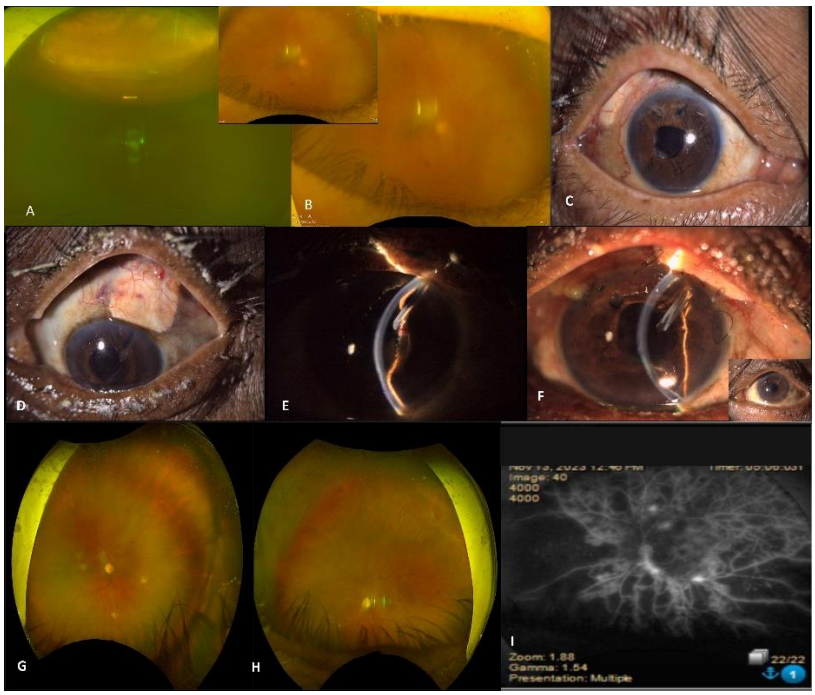

Figure1: A and B show the right and Left eye with bilateral proliferative diabetic retinopathy (case 1) with poor visibility in the right eye (A) owing to cataracts. C shows the postoperative outcome after Ahmed's glaucoma valve surgery with cataract surgery-Inset shows the postoperative retina showing regression of new vessels.

D-I shows the preoperative slit lamp photograph of case 2, D shows the postoperative picture showing the Ahmed glaucoma valve with patch graft and tube in a formed anterior chamber, the subsequent visit shows a flat chamber owing to straining, and F shows the picture after AC reformation. G and H show the retinal findings at the final follow-up after the retinal laser and E show the ischemic areas on fluorescein angiography.

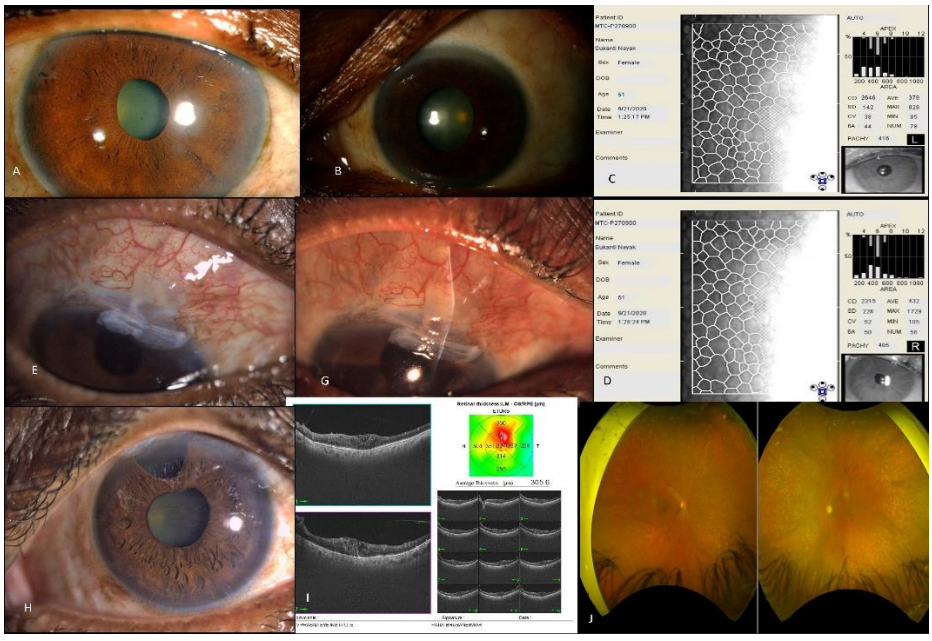

Figure 2: A-G shows the clinical details of case 5 with irido corneo endothelial syndrome and neovascular glaucoma. A and B show the preoperative clinical picture with C and D showing the endothelial changes in both eyes on specular microscopy. E and G show the postoperative photograph showing functional bleb after trabeculectomy with mitomycin-C with intravitreal bevacizumab with no visible hemorrhages or new vessels in the retina at the final follow-up. H-J shows the clinical picture after trabeculectomy with mitomycin-C with intravitreal bevacizumab in case 6 with persistent macular edema mandating additional injections and add-on laser. J shows the retinal details at the final follow-up after the completion of the laser showing resolution of macular edema.

Discussion:

This study of optimal surgical outcomes with patient-tailored strategies for concurrently addressing retinal ischemia and IOP control, which could salvage vision in all 6eyes. The IOP reduced significantly in all eyes, with one eye requiring AGM at the final follow-up. The retinal status was stabilised in all eyes, with 2 eyes requiring anti-VEGF for persistent macular edema. Five eyes achieved at least better than 20/400 vision, with one eye with advanced PDR and ischemic macula achieving a BCVA of 20/600.

Eyes receiving at least one anti-VEGF injection or pan-retinal photocoagulation (PRP) session within the first week demonstrated an association with achieving vision of 20/200 or better after 6 months in one study analysing 217 NVG eyes [8]. Recommendations emphasize the combination of PRP and anti-VEGF for effective outcomes in NVG [2,6,9-12]. However, consensus is lacking on combining retinal and glaucoma procedures in NVG, and there is limited evidence regarding practice patterns in retina or glaucoma clinics [2,6]. A study has shown favorable outcomes when glaucoma and retina specialists collaborate closely to address retinal ischemia and IOP [8].

The pharmacokinetics of bevacizumab and other anti-VEGFs indicate that the onset of action can be observed as early as 12 hours after intravitreal injection, with the aqueous concentration reaching 1.2mg within 3 days to 1 week, especially with higher doses [13-17]. This rapid onset of action suggests that concurrent use with filtering surgery may be considered in cases of acute neovascular glaucoma (NVG) characterized by fine, thread-like new vessels over the iris or angle [1,2,6]. The simultaneous control of IOP and the swift action of anti-VEGFs enables stabilization of both retinal and glaucoma risk factors enabling better visualization for laser PRP and a better surgical outcome. This strategy, observed in our cases, may be employed in specific situations to preserve useful vision in the better eye, requiring fewer follow-ups. The combined strategy of addressing the IOP and the retinal ischemia in the same sitting rapidly neutralizes the VEGF load in the anterior and posterior segment thereby hastening the therapeutic response after surgery in these situations. However, complete ablation of the skipped areas including the peripheral retina with multiple laser PRP under direct visualization after the combined procedures is crucial for a sustained reduction of the VEGF levels and control of the underlying cascade of events in retinal ischemia. Combined control of IOP and retinal ischemia also offsets the counterproductive effect of cataract surgery that allows easy access of pro-angiogenic factors into the AC [4,7].

Anti-VEGF medications are often administered prior to pan-retinal photocoagulation (PRP) or any filtering surgery for prompt regression of neovascularization due to their rapid onset of action [2,4,6,7,9,11,12,18,19]. This approach aims to minimize the risk of intraoperative or postoperative bleeding by lowering intraocular pressure (IOP). However, in our cases, none exhibited significant hyphema necessitating AC wash or additional procedures. Most cases presented with trace or less than one-third hyphema, which resolved with conservative management over time. While it is prudent to analyse the type of surgery offered based on a case-to-case basis in NVG and adopt a traditional step-wise approach to managing NVG, special scenarios like those seen in this cohort may mandate combined strategies which may also help salvage useful vision in these patients. Traditional stepwise algorithms, influenced by factors such as delayed presentation, bilaterality, poor vision in the other eye, financial constraints, and patients traveling from distant locations, can lead to delays in care and loss of follow-up, resulting in blindness in the only seeing eye. While they may be preferred in situations with early onset and presentation, the presence of dilated and engorged new vessels in the angle, or in cases where the media is clear, combined strategies to address both retinal ischemia and IOP can help achieve comparable surgical outcomes in atypical clinical scenarios.

There is a pressing need to establish standardized protocols for treating neovascular glaucoma (NVG) in both its acute and chronic phases. The diverse causes, varied clinical presentations, and differing demographic profiles of patients at the time of diagnosis present challenges in creating universally applicable treatment algorithms for all stages of NVG [2,6]. While a stepwise approach to NVG

management during hospitalization is recommended, certain situations may necessitate combined procedures for which a consensus has not been reached. Physical admission for the completion of all procedures may not always be feasible, particularly in private settings, or cases with unstable systemic conditions. This study suggests the potential benefits of combining retinal and glaucoma procedures for improved control of IOP and ischemia, presenting a novel approach to NVG management. Further research is warranted to investigate the long-term outcomes and compare the efficacy of different combinations of retinal and glaucoma interventions. This study underscores the potential favorable outcome of combining retinal and glaucoma procedures, which proved instrumental in preventing blindness, achieving IOP control, and concurrently stabilizing the retina.

Our study had several limitations. This was a non-comparative study with short-term outcomes. All our patients had good systemic control of diabetes or hypertension, which allowed us to intervene early. We excluded those with other forms of NVG owing to different treatment regimens for OIS or tumors/trauma to see the efficacy in specified pathogenic conditions only. Nevertheless, we believe a tailored approach of combined strategies applied on a case-to-case basis can help prevent blindness in NVG with cataracts, uncontrolled IOP, and poor view of the retina.

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