

Role of Intracameral Bevacizumab in combination with and without Panretinal Photocoagulation (PRP) in Neovascular Glaucoma Patients in our population

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ABSTRACT

Aim: To assess the efficacy of Intracameral (bevacizumab) in combination with and without pan retinal photocoagulation (PRP) in regressing anterior chamber iris and angle neovascularization and stabilizing IOP and improving outcome of secondary neovascular glaucoma in patients with proliferative retinal ischemic disorders in our population.

Methods: A Prospective, consecutive, interventional case series study was conducted at AFIO RWP and CMH Khuzdar on a series of patients 25 to 70 years of age. Thirty patients (30 eyes) with NVG secondary to ischemic retinal disorders were enrolled in the study design. The study group included 18(60%) males and 12 (40%) females. Cases were divided into two groups (A, B) and written informed consent was taken prior to procedure. Group A (15 patients) were managed with Intracameral bevacizumab alone While group B (15 patients) received laser pan retinal photocoagulation in addition to Intracameral bevacizumab. Majority had proliferative diabetic retinopathy (21 cases) and remaining nine cases were secondary to ischemic central retinal vein occlusion (CRVO). Baseline records were documented after carrying out complete ophthalmic evaluation in all patients. Follow up was carried out for 03 to 06 months depending on patient compliance.

Results: Significantly better reduction of Iris (rubeosis) and anterior chamber angle neovascularization and stabilizing of IOP was observed in Group B who received PRP in addition to Intracameral bevacizumab as compared to group A who were managed with Intracameral bevacizumab alone. Moreover early remission of neovascularization was observed in group A receiving bevacizumab only.

Conclusions: Combined procedures seems to be more effective in regressing and stabilizing iris/angle neovascularization, and lowering IOP in patients with NVG particularly in advanced cases.

Keywords: Bevacizumab, pan retinal photocoagulation, iris neovascularization, anterior chamber angle neovascularization,

INTRODUCTION

Neovascular glaucoma (NVG) is a relatively common condition characterized by rubeosis (iris neovascularization) and later on secondary angle closure glaucoma¹. In NVG formation of iris neovascularization (NVI), gradually progress to form a fibro vascular sheet on the surface of the iris and angle which later on contracts slowly and closes the angle, thus impairing aqueous outflow in trabecular meshwork thereby elevating the intraocular pressure (IOP), which if left untreated often leaves the patient with a painful and blind eye^{2,3}. Anterior Segment neovascularization results from various ocular and systemic diseases especially proliferative diabetic retinopathy and central retinal vein occlusion. Chronic

diffuse retinal ischemia seems to be the common postulated aetiological factor. Other patho-physiologic mechanisms such as chronic intra ocular inflammation, long standing retinal detachment, intraocular tumors and carotid obstructive disease may also lead to this disease⁴. Tripathi et al have shown that patients with underlying ischemic retina had significantly increased levels of vascular endothelial growth factor (VEGF) in aqueous humor which in turn stimulates iris and angle neovascularization⁵.

To date, laser pan retinal photocoagulation (PRP) is taken as gold standard in treatment of NVG. Retinal ischemia is reduced after PRP, which in turn decreases the level of VEGF, regression of neovascularization and control of NVG. Recently various studies using anti-VEGF agents in the management of NVG have been described⁶⁻¹⁰. Bevacizumab a humanized monoclonal antibody to VEGF, in a series of studies was reported to have a

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beneficial response in regressing retinal and iris neovascularization and control of IOP in neovascular glaucoma of various etiologies⁸⁻¹².

The aim of our study was to assess the efficacy of Intracameral bevacizumab in combination with and without pan retinal photocoagulation in neovascular glaucoma patients in our population.

MATERIAL AND METHODS

Thirty patients (30 eyes) with INV or NVG secondary to ischemic retinal disorders were included in the study design. The study group included 18(60%) males and 12 (40%) females (Table 1) aged 25 to 70 years. Out of the 30 cases, 21 (70%) had proliferative diabetic retinopathy and remaining 9(30%) cases were secondary to ischemic central retinal vein occlusion (CRVO) (Table 2).

Complete baseline ophthalmic examination was carried out included assessment of visual acuity by snellen charts, slit-lamp examination of the anterior segment, gonioscopy, applanation tonometry, indirect ophthalmoscopy and finally fluorescein angiography of iris neovascularization. Diagnosis of NVG was established on the basis of iris neovascularization/ angle neovascularization, raised IOP. Due to hazy media disc could not be adequately visualized in every case. Also, visual field examination could not be done in any of our patients due to poor visual acuity.

Cases were divided into two groups (A, B) and written informed consent was taken prior to procedure. Group A (15 patients) received Intracameral injection of bevacizumab (Avastin), 2.5 mg in 0.1 mL. The following protocol was used for injection: Eye speculum application, disinfection of conjunctival sac with povidone iodine 5%, anterior chamber paracentesis and then the Intracameral injection of bevacizumab. While group B (15 patients) received laser pan retinal photocoagulation in addition to Intracameral bevacizumab in a dose 2.5mg in 0.1 mL. The patients were followed weekly for 02 months then monthly up to 06 months. At each

Group B (15 patients) who received laser pan retinal photocoagulation in addition to Intracameral bevacizumab (Table 4) showed marked regression of the iris/angle neovascularization clinically in almost all eyes as compared to Group A (15 patients) who received Intracameral injection of bevacizumab (Table 3) only. Early remission and greater number of reoccurrence of neovascularization was observed in group A (Table 3) receiving bevacizumab only. Moreover regression takes longer time in group A

visit the best corrected visual acuity, slit lamp examination, applanation tonometry, gonioscopy and fundus examination were performed.

The regression of iris and angle neovascularization and the time to regression, presence or absence of recurrence were carefully documented. Recurrences were managed by additional PRP or by combining PRP with IVB.

RESULTS

Out of 30 patients who were identified to have rubeosis and neovascular glaucoma, NVG was secondary to PDR in 21 (70%) cases and to CRVO in 09 (30%)cases. 18 (60%) patients were males and 12 (40%) were females. The mean age of the patients was 58 years, with a range from 25 to 70 years. The mean follow up period was 03 to 06 months. Pre operative visual acuity ranged from 6/60 to perception of light with acceptable projection. Mean IOP ranges between 32-55 mm Hg with or without medication. Iris neovascularization was grade-4 clinically in 19 patients and grade 03 in remaining 11 patients. Gonioscopy showed variable degree of closed angles with peripheral anterior synechiae (PAS) involving 04 quadrants in 09 patients, PAS involving 03 quadrants in 07 patients and PAS involving one quadrant in 11 patients. The angle neovascularization involving two quadrants was found in 03 patients. Disc examination showed a CD ratio of 0.5 to 0.9 in 23 patients and in the remaining cases discs could not be adequately visualized due to poor visibility.

Table 1: Socio demographic profile of subjects

Gender	Frequency	%age
Male	18	60
Female	12	40

Table 2: Disease responsible for neovascularization

Etiology	Frequency	%age
Diabetes Mellitus	21	70
CRVO	09	30

(40-55 days) as compared to group B (15-22 days) in terms of number of days.

Although significant lowering of IOP was observed in both groups, a more stable IOP lowering effect was seen in the combined group. (Group B)

Table 3 and 4 shows patient data of group A and B, initial and final IOP, cases with reoccurrence, and additional adjunctive procedures like Drainage Valve/drops/ Cyclodestruction as required.

Table 3: Patient data (Group A) Avastin inj

Case no	Gender	Eye	Etiology	IOP mm of Hg		INV Grade	Re-occurrence	Drainage Valve/ drops/ Cyclodestruction
				initial	final			
1	M	OS	DM	35	18	3		Y
2	F	OD	DM	42	14	4	+	Y
3	M	OD	CRVO	40	17	4	+	Y
4	M	OS	DM	32	12	3		Y
5	F	OD	CRVO	46	15	4	+	Y
6	M	OD	DM	55	30	4	+	Y
7	M	OS	DM	49	18	4	+	Y
8	F	OS	DM	38	12	3		Y
9	M	OD	CRVO	34	14	4	+	Y
10	F	OD	DM	36	16	3		Y
11	M	OS	DM	44	19	4		Y
12	F	OD	DM	52	27	4	+	Y
13	M	OS	CRVO	42	16	4		Y
14	F	OD	DM	38	11	3	+	Y
15	M	OS	DM	48	20	4	+	Y

Table 4: Patient data (Group B) Avastin inj+PRP

Case no	Gender	Eye	Etiology	IOP mm of Hg		INV Grade	Re-occurrence	Drainage Valve/drops/ Cyclodestruction
				initial	final			
1	F	OD	DM	36	10	3		Y
2	M	OD	CRVO	42	13	4	+	Y
3	M	OS	DM	34	14	3		Y
4	M	OD	DM	52	24	4	+	Y
5	F	OS	CRVO	46	15	4		Y
6	F	OS	DM	32	11	3		N
7	M	OD	DM	44	16	4	+	Y
8	M	OD	CRVO	38	12	4		Y
9	F	OD	DM	40	15	3		Y
10	M	OS	DM	36	14	4		Y
11	M	OD	CRVO	46	18	4	+	Y
12	F	OS	DM	42	14	4		Y
13	M	OD	DM	34	10	3		Y
14	M	OS	DM	50	21	4	+	Y
15	F	OS	CRVO	36	16	3		N

DISCUSSION

Neovascular glaucoma (NVG) is a devastating complication of many ocular ischemic disorders, almost all of which are invariably associated with retinal ischemia.¹³ Despite recent advances mentioned in literature up till now there is no up to the mark satisfactory treatment protocol for the management of neovascular glaucoma. In unfortunate cases that develop neovascular glaucoma, meticulous screening early diagnosis and efficient control of IOP is of paramount importance to prevent visual loss and maintain useful vision. In order to improve treatment outcome of NVG cases it is essential to early detect iris and angle neovascularization and promptly address the underlying ischemic process responsible for the occurrence of rubeosis.³ In the past PRP was the standard treatment protocol followed for retinal ischemia, but as more studied are going on the

subject various alternative method/ combined procedures are making their way in the literature whose efficacy and safety is still yet to be worked out. The final aim of therapy should be a comprehensive management plan taking into consideration visual potential of the patient as well as patient comfort in case visual status is poor.

Intraocular Inj Avastin (bevacizumab) had been used in the past as an adjunct modality in anterior segment neovascularization of various etiologies^{9,10,12} Grisanti et al described 6 eyes with PDR and NVG in which early regression of NVI occurs following Intracameral injection of Bevacizumab with no relapse at four week.¹¹ Kahook and colleagues were the first who analyzed the role of intraocular bevacizumab in a case of NVG with uncontrolled IOP, who was on maximal medical therapy and cyclophotocoagulation¹⁴.

Our limited study shows that Group B (15 patients) receiving combined therapy (laser pan

retinal photocoagulation + Intracameral bevacizumab (Table 4) showed marked regression of the iris/angle neovascularization clinically in almost all eyes as compared to Group A (15 patients) who received Intracameral injection of bevacizumab (Table 3) only. Greater number of reoccurrences with early remission of neovascularization was observed in group A (Table 3) receiving bevacizumab only. Moreover regression time was longer in group A as compared to group B in terms of number of days. Although reasonable decrease of IOP was observed in both Group A&B, a better and stable control of IOP was seen in group B compared to group A.

To conclude, our study supports various studies in literature in terms of beneficial effect of bevacizumab when combined with PRP in regressing anterior segment neovascularization in our patients. Our limited research suggests that Intracameral bevacizumab when combined with adjunctive procedures like PRP definitely plays a positive role in early regression of iris and angle neovascularization thereby stabilizing the neovascular process and giving better control of disease.

CONCLUSIONS

Combined treatment like laser pan retinal photocoagulation and Intracameral bevacizumab resulted in more rapid decrease in IOP. In addition, the combined group had increased frequency and rapidity of regression of neovascularization thereby providing a better control over ischemic process. Since many cases require additional medical or surgical intervention to lower IOP or repeat injection of bevacizumab these cases should be monitored thoroughly and regularly. This study provides a basic foundation for further research and suggests a possible new approach for the treatment of NVG. Extensive future studies are required to improve final outcome for the service of humanity. Moreover pathology behind ischemic stimulus must be addressed in each and every individual separately.

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