

Original research article

A prospective observational study to identify the most common cause and the frequent stage of presentation in patients with neovascular glaucoma

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Abstract

Aim: To identify the most common cause and the frequent stage of presentation in patients with neovascular glaucoma.

Materials and Methods: A prospective observational study was conducted in the Department of RIO, Indira Gandhi Institute of Medical Science, Patna, Bihar, India, for 1 year. Total 100 eyes of 90 patients having neovascular glaucoma in one eye or both the eyes were included in the study. All patients underwent thorough ocular examination i.e., visual acuity, slit lamp bio-microscopy, intraocular pressure (IOP) measurement by Goldman applanation tonometry, gonioscopy with Posner 4 mirror indirect gonioscope and dilated fundus examination.

Results: The present study was conducted in 100 eyes of 90 patients out of which 80 patients had either eye involvement and 10 patients had both eyes involvement. All Patients were aged between 13-69 years with a mean of 54.63 ± 12.5 years. Out of 90 patients, 75 (83.33%) were males and 15 (16.67%) were females. The range of intraocular pressure (IOP) was 3-72 mm of Hg with mean of 29.52 ± 11.3 mm of Hg. On gonioscopic examination, most of the cases i.e., 54 (54%) had only rubeosis iridis without involvement of the angle, 19 (19%), 12 (12%), 7 (7%), 6 (6%) had neovascularization of angle (NVA) in one; two, three and four quadrants respectively. 3 cases had hyphema. In the present study, most of the patients i.e., 54 (54%) presented in rubeosis iridis stage, 31 (31%) in angle closure stage and 15 (15%) in open angle stage. Out of 100 eyes, 55 (55%) had diabetic retinopathy in variable severity, 12 (12%) had inflammatory etiology, 10 (10%) had retinal vein occlusion and 10 (10%) had glaucoma (PXG and absolute glaucoma).

Conclusion: In the present study, it was found that Proliferative diabetic retinopathy is the most common cause and rubeosis iridis is the most common stage of presentation in NVG.

Keywords: glaucoma, tonometry, gonioscopy, diabetic retinopathy

Introduction

Neovascular glaucoma (NVG) is a potentially blinding, intractable secondary glaucoma, characterized by the development of new vessels on the iris and/or angle, often resulting in

poor visual outcome if not detected and treated aggressively. In 1906, Coats described the histological appearance of new vessels on the iris in a case of central retinal vein occlusion (CRVO).¹ Panretinal photocoagulation has been shown to significantly reduce or eliminate anterior neovascularization and may reverse IOP elevation in the open-angle glaucoma stage. When the IOP begins to rise, medical therapy is required to control the pressure during the open-angle glaucoma stage. The mainstays of the therapy at this stage are drugs that reduce aqueous production such as carbonic anhydrase inhibitors, topical beta-blockers and alpha agonists. Although surgical intervention is often necessary, trabeculectomy alone and other shunt-tube drainage procedures for NVG are challenging because new vessels tend to recur, bleed easily, are always associated with postoperative inflammation and have higher rate of failure to control IOP.⁽²⁾ Recent case series have demonstrated a role for bevacizumab in reducing rubeosis iridis and as an adjunct treatment for NVG.²⁻⁴ The formation of new vessels is influenced by imbalance between pro-angiogenic factors (such as, vascular endothelial growth factor-VEGF) and anti-angiogenic factors (such as pigment-epithelium-derived factor).⁵ VEGF plays an important role in formation of new vessels in patients with ischemic retinal diseases.⁶ VEGF and insulin growth1 factors are produced by Mueller cells, retinal pigment epithelial cells, retinal capillary pericytes, endothelial cells and ganglion cells.⁷ Accumulation of Insulin growth-1 factor in aqueous humor causes rubeosis iridis and later the formation of adhesions between cornea and iris block the aqueous humor drainage.⁸ VEGF concentration decreases after the regression of new vessels.⁹ The non-pigmented ciliary epithelium is the major site of synthesis of VEGF in patients with NVG.¹⁰ Increased Interleukin-6 was noted in the aqueous of patients with NVG secondary to central retinal vein occlusion.¹¹ Studies have shown increased levels of basic fibroblast growth factor (bFGF),¹² transforming growth factor-beta1 and beta 2,¹³ nitric oxide,¹⁴ endothelin¹⁵ and free-radicals such as the superoxide¹⁶ in the aqueous humor of patients with NVG. Normal iris vessels have nonfenestrated endothelial cells with tight intercellular junctions whereas new vessels are thin walled without muscular layer or supporting tissue. New vessels show basement membrane changes, gaps and fenestrations in the endothelial cells on electron microscopy.^{17,18} The new vessels are mostly accompanied by a fibrovascular membrane consisting of proliferating myofibroblasts.¹⁹

Material and Methods

A prospective observational study was conducted in the Department of RIO Indira Gandhi Institute of Medical Science, Patna, Bihar, India for 1 year.

Methodology

After taking informed consent detailed history was taken from the patient or the relatives if the patient was not in good condition. The technique, risks, benefits, results and associated complications of the procedure were discussed with all patients. Total 100 eyes of 90 patients who underwent ophthalmological examination and diagnosed as having neovascular glaucoma were include in this study. All patients underwent thorough ocular examination i.e., visual acuity, slit lamp bio-microscopy, intraocular pressure (IOP) measurement by Goldmann applanation tonometry, gonioscopy with Posner 4 mirror indirect gonioscope and dilated fundus examination with +90 D lens. Neovascularization of iris (NVI) was identified as tuft of new vessels on iris mostly at the pupillary margin in an undiluted state, presence of ectropionuveae, hyphema was also observed. A single tonometer used throughout the study and IOP was measured by a single person throughout the study. Indirect ophthalmoscopy or B-Scan was done in eyes with hazy media due to corneal edema and/or dense cataract. Gonioscopy was done to identify new vessels and to grade the angle as open or closed. The number of quadrants with new vessels in the angle were noted.

Statistical analysis

The data collected was entered in excel sheet and is analyzed using SPSS version 20.0. Descriptive variables were given with frequency (percentage) or mean (standard deviation). The association of various variables like Cause of NVG with stage of NVG and stage of NVG with IOP were analyzed using appropriate parametric and non-parametric tests like chi-square test (p-value) and ANOVA- test

Results

The present study was conducted in 100 eyes of 90 patients out of which 80 patients had either eye involvement and 10 patients had both eyes involvement. All Patients were aged between 13-69 years with a mean of 54.63 ± 12.5 years. Out of 90 patients, 75 (83.33%) were males and 15 (16.67%) were females. The range of intraocular pressure (IOP) was 3-72 mm of Hg with mean of 29.52 ± 11.3 mm of Hg. IOP of 2 mm of Hg was noted in 10 patients out of whom 4 had chronic retinal detachment, 3 had chronic uveitis and 3 had vitreous haemorrhage with combined rhegmatogenous and tractional retinal detachment. IOP of 72 mm of Hg was noted in 6 cases which had proliferative diabetic retinopathy. IOP < 10 mm of Hg IOP was noted in 30 out of 100 eyes of which 4 had chronic uveitis, 5 had retinal detachment, 17 had diabetic retinopathy in variable severity, 2 had central retinal vein occlusion and 2 underwent parsplanavitrectomy. >50 mm of Hg IOP was noted in 15 eyes out of which 5 had CRVO, 4 had PDR, 3 had PDR and VH, 2 had chronic uveitis and 1 had chronic pseudoexfoliative glaucoma.

On gonioscopic examination, most of the cases i.e., 54 (54%) had only rubeosis iridis without involvement of the angle, 19(19%), 12 (12%), 7 (7%), 6 (6%) had neovascularization of angle (NVA) in one; two, three and four quadrants respectively. 3 cases had hyphema. In the present study, most of the patients i.e., 54(54%) presented in rubeosis iridis stage, 31 (31%) in angle closure stage and 15 (15%) in open angle stage (Table 2).

Table 1: Demographic profile of patients

Gender	Number of patients	%
Male	75	83.33
Female	15	16.67
Age in years		
Below 20 years	6	6.67
20-30	16	17.78
30-40	32	35.56
40-50	24	26.67
Above 50	12	13.33

Table 2: Stage of NVG

Stage of NVG	Number eyes	%
Angle closure stage	31	31
Open angle stage	15	15
Rubeosis iridis	54	54
Total	100	100

Table 3: Causes of NVG

Cause	Number eyes	%
Chronic RRD	2	2
DR	55	55
Glaucoma	10	10
Inflammation	12	12
S/P PPV	1	1
Vein occlusion	10	10

Chronic Rhegmatogenous Retinal Detachment, DR – Diabetic retinopathy, Glaucoma – pseudoexfoliative glaucoma (PXG) and absolute glaucoma, Inflammation – Chronic uveitis, Vasculitis and Eales disease, S/P PPV – status post parsplanavitrectomy, Vein occlusion – central retinal vein occlusion and branch retinal vein occlusion.

Out of 100 eyes, 55 (65%) had diabetic retinopathy in variable severity, 12 (12%) had inflammatory etiology, 10 (10%) had retinal vein occlusion and 10 (10%) had glaucoma (PXG and absolute glaucoma) (Table 3).

Table 4: Mean IOP in three stages of NVG

Stage of NVG	Mean IOP (mm of Hg)
Angle closure stage	36.87±15.267
Rubeosis iridis	23.95±14.715
Open angle stage	23.87±17.576

Compares the mean IOP in different stages of NVG. Mean IOP in Angle closure stage is significantly higher than the mean IOP in other two stages ($P = 0.000$). Whereas there is no statistically significant difference between the mean IOP in rubeosis iridis stage and open angle stage ($P = 0.869$). 61 eyes (61%) had IOP < 30 mm of Hg of which 52 were in rubeosis iridis stage. 39 eyes (39%) had IOP > 30 mm of Hg of which 31 were in angle closure stage. IOP < 30mm of Hg was found mostly in rubeosis iridis stage and > 30 mm of Hg was found in angle closure stage. On assessing the Cause of NVG in relation to stage of NVG ($P = 0.121$), 55 eyes (55%) had diabetic retinopathy in variable severity, of these 54, 31 and 15 were in rubeosis iridis, angle closure and open angle stage respectively.

Discussion

Neovascular glaucoma (NVG) is a form of secondary glaucoma characterized by formation of new vessels and proliferation of fibrovascular tissue on iris and in the angle. Slit lamp examination can reveal new vessels on iris, ciliary injection, corneal edema due to increase in IOP, anterior chamber reaction and ectropion uvea due to contraction of the fibrovascular membrane on the iris. Rubeosis can be missed in early stages as it can't be seen unless the iris is examined under high magnification in undiluted stage. New vessels on iris usually appear before the appearance of new vessels in angle but in rare conditions like ischemic central retinal vein occlusion, new vessels in the angle are seen without involvement of the iris. Therefore, it is very important to perform gonioscopy even though new vessels are not present on iris. Initially, the anterior chamber angle is open on gonioscopy but later, new vessels appear in the angle and in the final stages, due to formation of fibrovascular membrane and tissue contraction synechia can occur leading to synechial angle closure.²⁰

The present study was conducted in 100 eyes of 90 patients out of which 80 patients had either eye involvement and 10 patients had both eyes involvement. All Patients were aged between 13-69 years with a mean of 54.63 ± 12.5 years. Out of 90 patients, 75 (83.33%) were

males and 15 (16.67%) were females which is comparable to the study done by Vasconcelloset al.²¹ in which 46.16 % of the patients were between 60 and 79 years of age. In the present study, Out of 100 eyes, 55 (65%) had diabetic retinopathy in variable severity, 12 (12%) had inflammatory etiology, 10 (10%) had retinal vein occlusion and 10 (10%) had glaucoma (PVG and absolute glaucoma). It is comparable to the study done by Vancea PP et al.²² which states that 81% had NVG secondary to ischemic retinal changes and in another study done by Haefliger IO et al.²³ they found that the majority (97%) of cases are associated with hypoxia and retinal ischemia. The remaining 3% cases are secondary to inflammatory diseases like chronic uveitis and intraocular neoplasms. The commonest causes of NVG are Proliferative Diabetic Retinopathy (PDR) and central retinal vein occlusion. 55(55%) PDR is the most common cause of NVG in the present study and Vein occlusion 10%. The formation of new vessels is influenced by imbalance between pro-angiogenic factors (such as, vascular endothelial growth factor-VEGF) and anti-angiogenic factors (such as pigment-epitheliumderived factor). Studies have shown that increased levels of VEGF and decreased levels of PEDF was found in the vitreous of patients with proliferative diabetic retinopathy.^{24,25} In the present study 1 case who underwent pars planavitrectomy had developed NVG. Surgical intervention like pars planavitrectomy for PDR increases the incidence of rubeosis iridis.²⁶ Retinal hypoxia is frequently seen in proliferative retinopathies. A portion of oxygen from the aqueous humor diffuses posteriorly towards the hypoxic retina causing the iris hypoxia. This explains the risk of rubeosis after surgery like vitrectomy where oxygen reaches the ischemic retina faster leading severe iris hypoxia.²⁷ In our study 7 cases (7%) had NVG due to pseudoexfoliative material on iris. Studies found that pseudoexfoliative material gets deposited adjacent to the endothelial wall and causes thinning of the basement membrane, endothelial wall fenestration and reduction of lumen of the vessel thus causing iris hypoxia and ischemia leading to neovascularisation.^{28,29} In the present study 2(2%) had developed NVG due to chronic retinal detachment. Studies described NVG can develop rarely due to ischemia caused by chronic RD.^{30,31} In our study, most of the cases presented in rubeosis iridis stage followed by angle closure stage and open angle stage. In the present study, most of the patients i.e., 54(54%) presented in rubeosis iridis stage, 31 (31%) in angle closure stage and 15(15%) in open angle stage. In Rubeosis iridis stage most of the patients present with normal IOP and are usually asymptomatic. IOP begins to rise in Open angle glaucoma stage. In Angle closure glaucoma stage, IOP usually raises very high even up to 60 mmHg. Rubeosis may be severe with hyphema, anterior chamber reaction, conjunctival congestion and corneal edema.³² In the present study, the mean IOP in angle closure stage was found to be 36.87 ± 15.267 mm of Hg which is significantly higher than the other two stages ($P = 0.000$).

Conclusion

Neovascular glaucoma is a severe form of secondary glaucoma most commonly because of diseases causing retinal ischemia. So, early diagnosis and prompt treatment of the underlying retinal pathology can prevent neovascular glaucoma. In the present study, it was found that Proliferative diabetic retinopathy is the most common cause and rubeosis iridis is the most frequent stage of presentation in NVG.

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Received: 07-10-2020 || Revised: 06-11-2020 || Accepted: 22-11-2020