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Original Research Article

A Prospective Observational Identification of the Most Common Etiologies 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.

Material & Methods: The present study is a prospective observational study, 460 patients with Glaucoma of multiple type and of etiology underwent detail ophthalmological examination and 16 case those have been diagnosed as neovascular glaucoma (NVG) in one eye or both the eyes at Department of ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India over a period of 13 months were included in the study, with prevalence of 3.5% of all glaucoma cases.

Results: Most of the patients i.e., 11 (68.8%) presented in rubeosis iridis stage, 3 (18.75%) in open angle stage and 02 (12.5%) in angle closure stage. The Mean IOP in Angle closure stage was found significantly higher than the mean IOP in other two stages (P = 0.001).

Conclusion: In the present study, it was found although prevalence of NVG is significantly low among cases of all glaucoma but the rising trend of Diabetic in population is of concern and this study also confirms that more than half of the cases of NVG were found with Proliferative diabetic retinopathy is the most common cause and rubeosis iridis stage was the commonest finding.

Keywords: neovascular glaucoma, Secondary Glaucoma rubeosis iridis

Introduction

Anterior segment ischemia that lead to neovascularization of the iris and the anterior chamber angle are mainly caused by retinal ischemia and hypoxia due to an ocular ischemic diseases as central (CRVO) or branch retinal vein occlusion (BRVO), proliferative diabetic retinopathy (PDR) and other causes include sickle cell retinopathy, retinal embolic diseases, chronic retinal detachment and inflammatory conditions as uveitis and vasculitis, carotid stenosis and other uncommon causes that causes retinal hypoxia. [1] Retinal ischemia is associated with production of vascular endothelial growth factor (VEGF), Pigment epithelium derived factor (PEDF), basic fibroblasts growth factor (bFGF) and other angiogenic

factor which enhances retinal neovascularization, iris neovascularization and in severe cases, proliferation of fibrovascular membrane in the angle of anterior chamber which will lead to elevation of IOP and neovascular glaucoma. [2] Once the diagnosis of retinal hypoxia is established, the natural history of neovascular glaucoma can be divided to four stages: pre-rubeosis stage, preglaucoma stage, open-angle glaucoma stage and angle-closure glaucoma stage. 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 rubeosisiridis and as an adjunct treatment for NVG. [2-4]

Treatment of NVG has two main components: (1) management of IOP elevation and (2) reduction of the ischemic drive, traditionally through panretinal photocoagulation (PRP).[5] If applied early, PRP can induce regression of both anterior and posterior segment neovascularization. [6] However, the response to adequate PRP is often incomplete, [7-8] and effective laser treatment may be hampered by the presence of cloudy media secondary to corneal edema, hyphema, cataract, and/or vitreous hemorrhage. Moreover, the effects of PRP often takes several weeks to take effect; [9] during this window, angle closure and further ocular damage due to continually elevated IOP can occur.

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. [10-11] The new vessels are mostly accompanied by a fibrovascular membrane consisting of proliferating myofibroblasts. [12]

Thus, we aim to identify the most common cause and the frequent stage of presentation in patients with neovascular glaucoma.

Material & Methods:

The present study is a prospective observational study, 460 patients with Glaucoma (raised intraocular pressure) of multiple type and of etiology underwent detail ophthalmological examination and 16 case has been diagnosed as neovascular glaucoma (NVG) in one eye or both the eyes at a Patna Medical College and Hospital, Patna, Bihar, India. Over a period of 13 months were included in the study. Patients were explained about the study and informed consent for the same was obtained.

There was no financial interest in this study. There was no conflict of interest.

Relevant detailed medical and ocular history was obtained from all the patients.

All patients underwent thorough ocular examination i.e., visual acuity, slit lamp bio-microscopy at greater magnification, intraocular pressure (IOP) measurement by Goldmann applanation tonometry and with Schiotz tonometer in cases with absolute glaucoma cases or where applanation tonometry were not possible due to ill health of patient or not cooperative on slit lamp. Gonioscopy was performed with single mirror (62 degree angled)

gonioscope with help of viscous coupling and 4% cocaine as topical anesthesia. Fundal examinations were performed with +90 D lens on Slit lamp, 20D by indirect ophthalmoscopy and direct ophthalmoscope whichever was found suitable on individual basis.

Neovascularization on iris (NVI) was identified as tuft of new vessels on iris mostly at the pupillary margin in an undilated state, presence of ectropionuveae and hyphema was also noted [Figure 1A, 1B & 1C]

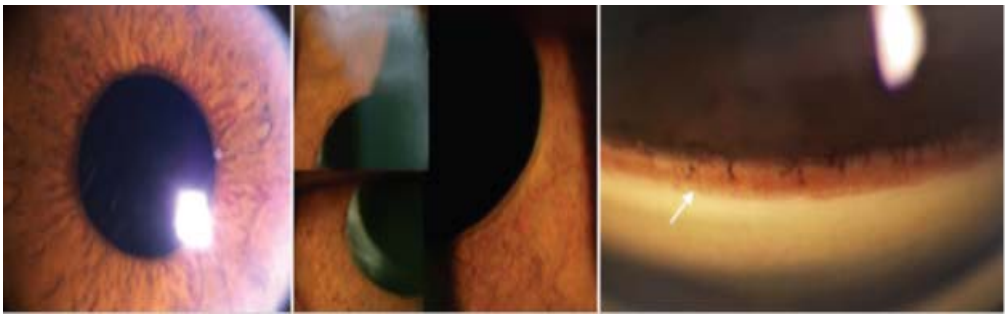

Figure 1A, 1B & 1C

A single applanation or Schiotztonometer (whenever required) were 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. In gonioscopy identification of new vessels in angle (NVA) and the number of quadrants with NVA was noted and also, the grading of Angle (open or closed) was observed and 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 460 patients of diagnosed cases of glaucoma, out of which 380 patients had both eye and 80 patients had eyes involvement. All Patients were aged between 34 ± 80 years with a mean of 55.72 ±12.45 years.

In the present study, out of 16 cases of NVG 11 (68.8%) presented in rubeosisiridis stage, 02 (12.5%) in angle closure stage and 3 (18.75%) in open angle stage.**[Table 1]**.

Table 1: Stage of NVG

Stage of NVG	N	%
Angle closure stage	02	12.5
Open angle stage	03	18.75
Rubeosisiridis	11	68.8
Total	16	100.0

Out of 16 eyes diagnosed with NVG in different stages, 10 (62.5 %) had diabetic retinopathy in variable severity, 3 (18.75 %) retinal vein occlusion, 2 (12.5 %) (PXG and absolute vein occlusion and glaucoma) and 1 (6.25%) had inflammatory etiology. **[Table 2]**

Table 2: Causes of NVG

Cause	n	%
Diabetic retinopathy	10	62.5
Inflammation	1	6.25
Retinal Vein occlusion	3	18.75
PXG and absolute glaucoma	2	12.5
Total	16	100.0

The mean IOP in Angle closure stage was significantly higher than the mean IOP in other two stages (P = 0.001). Whereas there is no statistically significant difference between the mean IOP in rubeosisiridis stage and open angle stage (P = 0.753). **[Table 3]**

Table 3: **Mean IOP in three stages of NVG**

Stage of NVG	Mean IOP (mm of Hg)
Angle closure stage	35.39 ±16.821
Rubeosisiridis	24.61 ±15.464
Open angle stage	22.54 ±18.380

Discussion:

Treatment of NVG depends on the stage of the disease. Early during the course of the disease, the goal is to ablate ischemic retina, thereby decreasing the ischemic drive and reducing the amount of VEGF released and neovessel formation. PRP appears to be effective in inducing regression of NVI and preventing the development of NVG if administered before the development of IOP elevation and if the amount of neovascularization over the angle is minimal. [13]

Ehlers et al [14] in their study of combination intravitreal bevacizumab and PRP vs PRP alone in the treatment of NVG. Although they showed a trend towards greater surgical interventions in the PRP only group, it was not statistically significant, and the mean initial IOP was lower in the combination group, which might have enhanced the apparent response to treatment. In another retrospective review by Wakabayashi et al, [15] repeat intravitreal injections of bevacizumab as an adjunctive modality to PRP appeared to reduce the rate of surgical interventions in eyes with open angles, although this did not reduce the rate of such interventions in eyes with closed angles.

There have a few literatures reporting the use of microstent EX-PRESS shunt in NVG. It is made of stainless steel, which is applied to ensure a new path for the removal of aqueous humor from the AC to the space under the Tenon's capsule. Although it has been demonstrated to be a safer and easier option for primary open-angle glaucoma with comparable IOP-control effects to trabeculectomy, actually it is not suitable for NVG angle closed stage as the progress of peripheral goniosynechia and short length of the shunt (3 mm). Even at early-stage NVG without angle closure, the success rate of EX-PRESS implantation is quite low if not controlling the underlying diseases. [16]

Study done by Vancea PP et al. [17] which states that 81% had NVG secondary to ischemic retinal changes and in another study done by Haefliger IO et al. [18] they found that the majority (97%) of cases are associated with hypoxia and retinal ischemia.

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 neovascularization. [9-20]

In Rubeosisiridis 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. Rubeosismay be severe with hyphema, anterior chamber reaction, conjunctival congestion and corneal edema. [21, 22]

Conclusion

In the present study, it was found although prevalence of NVG is significantly low among cases of all glaucoma but the rising trend of Diabetic in population is of concern and this study also confirms that more than half of the cases of NVG were found with Proliferative diabetic retinopathy is the most common cause and rubeosisiridis were the commonest finding and also, the most common stage of presentation in NVG. Early diagnosis could be a key of success to manage this type of glaucoma which can lead to blindness if left untreated till late.

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