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Review Article

Neovascular glaucoma- A review

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ABSTRACT

The objective of this review is to emphasize on basic and clinical aspects of Neovascular glaucoma (NVG) as it is a severely blinding and intractable disease. Therefore, to prevent or reduce the extent of visual loss caused by NVG, a detailed knowledge of its causes, pathogenesis, pathology, methods of early diagnosis and management is of utmost importance. The most common diseases responsible for development of NVG are ischaemic central retinal vein occlusion (CRVO), diabetic retinopathy and ocular ischaemic syndrome. In management strategy, the key point is to maintain a high index of suspicion of development of NVG in at risk patients and prevent its development with appropriate management of causative disease. If NVG develops, early diagnosis and its management by various medical and surgical means should be done at earliest. Management of NVG essentially consists of controlling high IOP by medical and or surgical interventions. Currently we still do not have a satisfactory option for treating NVG and preventing the profound loss of vision. This review basically discusses the various advantages and limitations of various medical and surgical techniques which are being commonly employed.

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1. Introduction

Among the different types of secondary glaucoma Neovascular Glaucoma (NVG) is one of the most dreaded complications to occur. The term neovascular glaucoma was first described by Weiss and colleagues in the year 1963.¹ Earlier several terms like congestive glaucoma, hemorrhagic glaucoma, rubeotic and thrombotic glaucoma were used.² Retinal ischaemia leads to neovascularization of iris and angle of anterior chamber and in later stages there may occur proliferation of fibrovascular tissue in the anterior chamber angle.³

The term neovascularization is used when new blood vessels are formed on those tissue which are not vascularised normally. The new vessels that are formed are weak and bleed easily subsequently lead to cellular infiltration. NVG is a very disastrous condition with a very aggressive course and leading to irreversible

deterioration of vision which may progress to complete loss of vision and intolerable ocular pain. Depending on the severity of neovascularization the angle of anterior chamber can be open resulting in secondary open angle glaucoma or closed due to secondary synechial angle closure leading to secondary closed angle glaucoma. NVG is very difficult to treat and response to medical management alone is ineffective, so a combination of medical and surgical treatment is done to lower the intraocular pressure and prevent any further deterioration of vision. The most important condition that leads to neovascular glaucoma is development of retinal hypoxia. The common condition which causes retinal hypoxia are central retinal vein occlusion (Ischemic type), diabetic retinopathy (proliferative type) and carotid occlusive disease.

1.1. Etiology

Normally various pro-angiogenic factors like vascular endothelial growth factor (VEGF) and anti-angiogenic

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factors like pigment epithelium derived growth factor (PEDF) work in harmony to maintain a homeostatic balance but when ocular tissue suffers from hypoxia due to diseases like veno-occlusive disease, diabetes, ocular ischaemic syndrome, the ischaemic retinal tissue starts releasing angiogenic factors predominantly VEGF which stimulates the process of neovascularization by activation, proliferation and migration of endothelial cells. Later on as the disease progresses a fibrovascular membrane is formed over iris and angle of anterior chamber which interferes with aqueous drainage and finally contracts in due course of time which causes anterior synechiae. Raised level of interleukin 6 which is an angiogenic factor has also been found in the aqueous humour of CRVO patients suffering from NVG.⁴

1.2. Clinical course

There are four stages of neovascular glaucoma:

1. Pre-rubeosis stage – Clinically new vessels on iris or angle cannot be seen in this stage.
2. Rubeosis stage – In this stage tiny tufts of new vessels can be seen at the pupillary margin of iris but the angle is not involved. IOP is usually normal at this stage.
3. Secondary open angle glaucoma stage – new vessels invade iris stroma and angle. On gonioscopic examination the angle will be seen open. The IOP may be normal or elevated.
4. Secondary angle closure glaucoma stage – the new vessels are extensive and there is an overlying fibrovascular membrane. Flattening and anterior displacement of the iris occurs, ultimately resulting in total synechial angle closure.

1.3. Diagnosis

Careful and thorough ophthalmological examination in an undilated pupil helps in the clinical diagnosis of NVG. The slit lamp examination of the anterior segment and Gonioscopy reveals the presence of new blood vessel on the iris along its pupillary margin and in the angle. With the advent of newer technology like anterior segment optical coherence tomography (ASOCT) and ultrasound biomicroscopy, the diagnosis and staging of the disease has become very easy and reliable and are most commonly used modalities. Due to its grave prognosis, early detection is most important step and therefore one should be always suspicious in all high risk patients.

1.4. Clinical feature

The clinical presentation of neovascular glaucoma may vary from few mild signs and symptoms to a numerous severe symptoms depending upon the stage:

1. Decrease in visual acuity – loss in sight is irreversible and in late stages complete loss of vision can occur.
2. Ocular pain
3. Intraocular pressure can be normal in early stage but is usually very high as the disease advances.
4. Redness of eyes
5. Corneal edema – as a result of raised IOP
6. Flare, cells and posterior synechiae can be seen in anterior chamber.
7. Ectropion uveae
8. Subtle to extensive neovascularization of iris and angle.
9. Synechial angle closure on gonioscopy.

The earliest signs of NVG are the prominence of small tufts of new vessels at the margin of the pupil and dilatation of major arterial circle of the iris. In the process of neovascularization, the new vessels formed differs from the normal vessels in their anatomy, distribution and pattern of growth with the new vessels growing over the surface of iris in an irregular, zigzag pattern in contrast to the predominance of normal vessels being radially distributed in the stroma of iris.⁵ Anatomically, new vessels differ from normal vessels in terms of being thinner, having gap in their endothelial cells as seen by electron microscopy, deficiency in muscular layer, and changes in the basement membrane of retinal vessels in diabetic patients.^{6,7} On Gonioscopic examination in non mydriatic eyes, it becomes evident that the new fine arborized vessels crosses over scleral spur onto the trabecular meshwork whereas normally, vessels typically do not grow behind the sclera spur.⁸ As the disease progresses, a fibrovascular membrane is formed over iris and iridocorneal angle which may contract in later phase resulting in distortion of the normal architecture of iris, ectropian uveae, and synchae formation in the iridocorneal angle resulting in synechial angle closure.⁹

2. General Treatment

NVG being a disease with rapid progression and sight threatening potential requires a multifaceted approach aiming at the reduction of IOP to a desirable level and simultaneously treating the underlying disease that is responsible for increase production of vasoproliferative and growth factors promoting neovascularization.

Panretinal photocoagulation (PRP) using around 1500 to 2000 or more laser spots in 2 divided session is still the first and best treatment option to be used in all cases where retinal ischaemia is seen on funduscopy or in fluorescein angiography.¹⁰ PRP works by various mechanisms, amongst which one predominant way is the reduction of the amount of angiogenic factors required by ischemic tissue by photoablating that specified area. In certain cases because of a hazy fundus, PRP becomes very difficult and in these cases an alternative option is to do endocyclophotocoagulation along with pars plana Vitrectomy (PPV).

It has been found that an early use of anti-VEGF has a promising role in prompt elimination of neovascularization of anterior chamber.

Ranibizumab, bevacizumab and aflibercept are a few anti-VEGF agents widely used nowadays in the form of intravitreal injections to block the effect of VEGF and regress neovascularization. The effectiveness of intravitreal bevacizumab injection in controlling neovascularization along with its additive advantage of lowering IOP, reducing ocular pain, and lower cost in respect to other anti-VEGF injections available, makes it a popular choice for current use.¹¹ The quick action of bevacizumab in regressing the friable, leaky new vessels in iris and angle of anterior chamber within 24–48 hours as compared to 2–3 weeks required by panretinal photocoagulation, has led to its widespread use in NVG.

3. Medical Therapy

For the initial treatment of NVG topical medicine is helpful. In order to reduce IOP, at first those anti glaucoma drugs are used which act by decreasing the production of aqueous rather than those that increase uveo-scleral outflow because if the angles are closed then they will not be effective. Therefore beta blocker, carbonic anhydrase inhibitor (CAI) and alpha 2 adrenergic agonist eye drops are commonly used and prostaglandin analogue drugs are avoided. Pilocarpine has a propensity to increase inflammation, besides it causes miosis which is an undesirable effect as it will aggravate synechial angle closure and impede uveoscleral outflow, therefore this drug is contraindicated. If the IOP is still not controlled by topical drug and further reduction is required then systemic medications like hyperosmotic agents and oral acetazolamide can be added taking precaution regarding blood sugar level and kidney function status. The simultaneous use of topical and systemic CAI in adults to decrease aqueous production has not been found to be useful but can be effective in children.

4. Surgical Management

If the topical and systemic antiglaucoma drugs fails to control IOP and there is further deterioration in vision then surgical intervention is carried out.

Trabeculectomy along with antimetabolite therapy is a considerable step to control IOP. NVG associated severe inflammation often limits the success of trabeculectomy so the use of antimetabolite adjuvant to trabeculectomy has been found to have a better outcome rather than trabeculectomy done alone. The combined surgical approach of trabeculectomy with application of anti fibrotic agent and preoperative intravitreal injection of bevacizumab yields a very high rate upto 95%.¹²

5. Glaucoma Drainage Devices (GDD)

The indications of use of drainage devices occur when there is presence of excessive conjunctival scarring which leads to a high failure rate of trabeculectomy or when the primary trabeculectomy fails. The different drainage devices that are used include Molteno implant, Baerveldt implant and Ahmed glaucoma valve have been used with each of them having almost equal success rate.¹³

Among the complication, early post operative hypotony can occur soon after surgery. Late Post operative complication include blockage of the tube in the anterior chamber and fibrous encapsulation over the devices.

6. Cyclodestructive Procedures

Cyclodestructive procedures are used on those eyes where both medical and surgical treatment have become refractory and these eyes have a poor visual outcome. The procedure include cyclodestruction by transscleral cyclophotocoagulation with Nd:YAG or semiconductor diode laser can be considered. These procedures destroy the ciliary body and as a result aqueous humour production decreases. But hypotony and phthisis can occur if excessive tissue is destroyed.

In painful blind eyes, retrobulbar alcohol injection and even enucleation or evisceration can be justified.

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8. Conflict of Interest

The authors declare that there is no conflict of interest.

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