

Glaucoma A Multifactorial Disease and Its Multidimensional Management

Dr. Vishal Jindal

Panchkula Haryana India

Abstract- Glaucoma is a multifactorial optic neuropathy characterized by retinal ganglionic cell death. Elevated intraocular pressure (IOP) is a recognized risk factor for retinal ganglionic cell degeneration in glaucoma, but is it the only cause of glaucoma? Do progression of glaucoma is fully controlled by controlling IOP? No. Today there are enormous pharmacological and surgical methods to control IOP, but still progression of glaucoma is uncontrolled. It is the need of an hour to work into deeper details of glaucoma, to find its associations and find new multidimensional approach to treat glaucoma. In this article, we found some associations of glaucoma with various age related disorders, and new treatment modalities. This will widen our horizon of thinking and will enable us to find better therapeutic ways to control glaucoma.

Index Terms- glaucoma, alzheimer's disease, omega 3, exercise

I. INTRODUCTION

Glaucoma is a multifactorial optic neuropathy characterized by retinal ganglionic cell death. All the cells of our body are in a continuous cycle of death and renewal but the ganglionic cell death is irreversible, once damaged means lost forever. Therefore glaucoma is an irreversible disease. This irreversible ganglionic cell death results in progressive visual field loss along with decreased color sensitivity and contrast.

Elevated intraocular pressure (IOP) is a recognized risk factor for retinal ganglionic cell degeneration in glaucoma, but is it the only cause of glaucoma? Do progression of glaucoma is fully controlled by controlling IOP? No. Today there are enormous pharmacological and surgical methods to control IOP, but still progression of glaucoma is uncontrolled, visual field loss continue to progress. So there must be some other cause or risk factor.

This disease of glaucoma is quite similar to various other diseases of body like Osteoporosis, osteoarthritis, Alzheimer's disease, coronary artery disease¹, cataract etc. All of these are chronic age related degenerative diseases in which there is a continuous damage to some cells of body is occurring whether it is bones, neurons, joints or vessels wall. With age, the efficiency of all these structures is gradually reducing, and when they cross a certain threshold, symptoms start to appear in various forms like loss of memory, pain in joints, breathlessness and many more. Similarly its occurs in glaucoma, there is a chronic neurodegenerative process, which generally starts in middle age and then progress slowly without any signs and symptoms, as age advances, visual field continues to contract, then, one fine

day patient presents with blurring of vision, decreased color and contrast sensitivity and finally diagnosed as glaucoma.

These above mentioned diseases like osteoporosis¹, osteoarthritis²⁻³, coronary artery disease⁴⁻⁵, dementia's all can occur in young patients, can be genetically inherited, and also influenced by environmental and other factors, similar occurs in glaucoma, it can also be genetically inherited and can also occur in young age.

Alzheimer disease is a progressive neurodegenerative disease which present in form of dementia. Recent studies suggest that there is a significantly higher rate of glaucoma occurrence among patients with Alzheimer disease (AD)⁷⁻⁸. In AD there is loss of neurons in the hippocampus and cerebral cortex, leading to short-term memory loss. It is characterized by the formation of aggregated proteins composed of amyloid known as amyloid plaques, and neurofibrillary tangles, composed of hyperphosphorylated tau protein. . Interestingly, it has been reported that AD and glaucoma have many common features⁶. Sunderland et al. noted that levels of A β ₁₋₄₂ significantly decreased in cerebrospinal fluid from AD patients in comparison with control subjects⁹. Subsequently, we reported that levels of A β ₁₋₄₂ significantly decreased in the vitreous fluid from glaucoma patients in comparison with control subjects with macular hole¹⁰. On the other hand, a chronic elevation of IOP induces A β in RGCs in experimental rat glaucoma⁶. This result is consistent with some previous reports on experimental mouse glaucoma models¹¹⁻¹³. Furthermore, Guo et al. reported that neutralizing antibody to A β significantly delays and attenuates RGC apoptosis in experimental glaucoma¹¹. These findings indicate that A β ₁₋₄₂ neurotoxicity as AD brain may be involved in RGC death in glaucoma. Furthermore, progression of visual field defects is accelerated in patients with open-angle glaucoma and AD versus patients with open-angle glaucoma without AD¹⁴. Hyperphosphorylated tau protein has also been detected in the retinas of glaucoma patients¹⁵. So these studies and results showed that there is some association between these two diseases. Further studies are needed to clarify this relationship.

Lifestyle and healthy habits have significant effect in controlling the progression of these diseases like regular exercise decreases the chances of coronary artery disease¹⁶⁻¹⁷, regular intake of omega 3 fatty acids control Alzheimer's disease¹⁹, decreased mental stress and tension definitely control the progression of metabolic diseases. So all these above mentioned therapies should have some role in treatment of glaucoma.

Various studies have been conducted to evaluate the role of omega 3 fatty acids on IOP reduction and glaucoma progression. Ren et al.¹⁹ found decreased omega-3

polyunsaturated fatty acids (PUFA) levels in glaucoma patients compared with their healthy siblings, whereas Kang et al.²⁰ found that a lower omega-6, omega3 consumption ratio was associated with increased glaucoma prevalence. Nguyen et al.²¹. Demonstrates that increasing omega-3 PUFA consumption leads to decreased IOP with age through increased aqueous outflow facility. Further studies are needed to consider whether manipulation of dietary omega-3 fatty acids may be important in modifying the risk for chronic eye diseases such as glaucoma. It had been observed that physical exercises could reduce the intraocular pressure (IOP) in patients with glaucoma²². However, the effect of IOP reduction varied with exercise type and intensity, as well as the duration of exercise²³⁻²⁴. Difference of lowering the IOP in glaucoma patients and healthy people were also observed. The mechanisms of reducing the IOP by exercise were very complicated and believed to be associated with the lower concentration of nor epinephrine, the rising of colloid osmotic pressure, the co-action of nitric oxide and endothelin after exercise, and also related to the gene polymorphism of β 2-adrenergic receptor²²⁻²⁵. Overall, exercise has been found to lower IOP. Studies also have found that it improves blood flow to the retina and optic nerve. In one study, jogging for 20 minutes lowered IOP by 1 mm Hg to 8 mm Hg. Valsalva maneuver (the technical term for what happens when, after an inhalation, you hold your breath and apply pressure against your epiglottis), appears to have a negative impact on IOP. While few studies have been conducted on yoga and glaucoma, there is some evidence that inverted poses increase IOP²⁶. This includes headstand, shoulder stand and the plow. Currently, there are no cohort studies reporting the relationship between exercise and glaucoma; moderate aerobic exercise has many health benefits and thus should be encouraged.

A prolonged stress-induced increase in endogenous cortisol and catecholamines with subsequent alterations of the immune response may increase IOP²⁷⁻²⁸. So, it may be prudent to ask about potential psychosocial or environmental stress factors, especially in a patient who had stable disease and now has developed a dramatic rise in IOP or deterioration of visual function.

Caffeine is consumed by a high percentage of the general public. Most of the studies²⁹⁻³⁰, with some exceptions³¹, demonstrates 2 to 3 mm Hg increase in IOP that lasts for about 2 hours after use of coffee. However, coffee beans also contain compounds that have antioxidative effects³²⁻³³ these antioxidative effects and its possible neuroprotective implications need further research.

Ginkgo biloba and bilberry (shrubs that yield a fruit resembling blueberries) have been proposed as neuroprotectors. The main components of the Ginkgo leaf extract are flavonoid glycosides and terpene lactones. Ginkgo is thought to mediate its effects through several biological mechanisms including antiplatelet action, vasodilation, and antioxidant effect. There is little data regarding the effect of Ginkgo biloba on the course of glaucoma. A placebo-controlled randomized controlled trial (RCT) found that Ginkgo biloba improved preexisting visual field loss in some patients with normal tension glaucoma³⁴. Further research is mandatory before we start recommending use of ginkgo biloba along with conventional glaucoma therapy on a routine basis.

Glaucoma is an age-related, chronic neurodegeneration of the optic nerve. The molecular and cellular pathologies that characterize the disease are shared by other chronic neurodegenerations such as AD. Therapies directed at treating chronic neurodegenerations have potential for use in treating glaucoma; conversely, therapies that are successful in treating glaucoma could be used in treating other chronic neurodegenerations.

When patients inquire about the relationship between lifestyle factors, alternative medicine, and glaucoma, the physician should take the opportunity to educate them about their disease. Few activities should be avoided by the glaucoma patients, although more evidence is needed to determine if these activities predispose to glaucoma or contribute to the progression of the pre-existing disease. So we should widen our horizons and see into the deeper details of pathophysiology, etiology, and management options for glaucoma.

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AUTHORS

First Author – Dr. Vishal Jindal, H.No. 102 GHS 51 sector 20 Panchkula Haryana India, Email id- vishaljindal87@gmail.com, Phone no.- +918146446655