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<p>Website: www.e-tjo.org</p>
<p>DOI: 10.4103/tjo.tjo_71_20</p>



Is intraocular pressure reduction the key treatment for normal-tension glaucoma?

Normal-tension glaucoma (NTG) is a progressive optic neuropathy similar to primary open-angle glaucoma (POAG), but intraocular pressure (IOP) within the normal range (below 21 mmHg). Traditionally, glaucoma is regarded as a disease with elevated IOP. However, the presence of glaucoma under “normal” pressure is much more common than we thought. Its prevalence is particularly higher in Asia, where NTG represents 47%^[1] and 92%^[2] of cases with POAG. Whether it is caused by genetics or by the environment, there is still no answer. Due to the growth of aging population in Asia, NTG has become a major issue in ophthalmologic care.

The article by Chen in this issue described the latest information on epidemiology, the pathogenesis, and the diagnosis of NTG. The term “normal tension” is misleading because this disease occurs with the so-called “normal” IOP. While IOP is the major risk factor in POAG, NTG has more IOP-independent factors. Compared with high-pressure POAG, the development of NTG may be a result of a complex interaction of multiple ocular and systemic factors. Ocular and systemic vascular disorders^[3,4] may be one of the proposed pathogenic mechanisms. A low ocular perfusion pressure including a low systolic blood pressure seems to be the cause for optic neuropathy in NTG. Higher translaminal pressure gradient due to impaired cerebrospinal fluid dynamics^[5] may also account for the disease.

It is important that NTG is a diagnosis by excluding other nonglaucomatous optic

neuropathies. To evaluate patients, a detailed history taking must include systemic medical conditions and medicines, family history of glaucoma, and history of ocular surgery or trauma. A thorough ophthalmic examination should include best-corrected visual acuity, refraction, central corneal thickness, slit-lamp examination, Goldmann applanation tonometry, gonioscopy, fundus photography, and standard automated perimetry. Optical coherence tomography is highly suggested to evaluate the optic nerve head, retinal nerve fiber, and ganglion cell complex. Diurnal IOP measurement should be performed to confirm the constantly low IOP and avoid missed IOP peaks.

The purpose of glaucoma treatment is to prevent the onset and development of the disease and maintain visual function throughout the patient’s life. How to treat NTG? What is the role of IOP reduction in the treatment for NTG? The article by Jayaram in this issue described the significance of every 1 mmHg of IOP lowering to reduce both the risk of developing glaucoma and the progression of the existing disease. From the evidence supported by well-designed, large randomized controlled clinical trials, IOP reduction remains the mainstay of treatment in NTG.^[6] The Collaborative NTG study randomized patients to 30% IOP reduction from baseline or no treatment. After 5 years, the study showed that a 30% IOP lowering reduced the risk of visual field progression to 12% in the study group compared to 35% in the control arm.^[7] The Early Manifest Glaucoma Trial showed that a 25% IOP lowering can also reduce the risk of disease progression to 45% in the study group compared to 62% in the control group

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How to cite this article: Chen MJ. Is intraocular pressure reduction the key treatment for normal-tension glaucoma? Taiwan J Ophthalmol 2020;10:241-2.

Submission: 03-10-2020
Accepted: 10-10-2020
Published: 20-11-2020

after 6 years of follow-up.^[8] IOP reduction is currently considered to be the only known modifiable risk factor for glaucoma, even when the IOP is within the normal limit.

Because NTG has more IOP-independent factors, how do we use IOP-independent therapy? A review of the literature reveals information concerning about neuroprotection and vascular maintenance. Cardiovascular health should be considered first. Patients should avoid the use of nonselective topical β -blockers and any systemic antihypertensive at night. Patients need to control blood sugar and hyperlipidemia. Regular exercise and having a diet rich in antioxidants is highly recommended. In addition, consider using “herbal” supplements with caution, such as Ginkgo biloba and resveratrol.^[9]

In conclusion, NTG has structural and functional damage similar to POAG, but IOP within the normal range. NTG is more prevalent in Asia than in Western countries. Due to the increasing elderly population and underdiagnoses in clinical settings, NTG has become a great challenge for Asian ophthalmologists. The complexity of the pathophysiology has included some IOP-independent risk factors. Therefore, IOP-independent therapy may be beneficial for NTG, but requires further investigation. For now, reducing IOP as low as possible (with medication, laser trabeculoplasty, or surgery) is the key to manage NTG patients.

Financial support and sponsorship

Nil.

Conflicts of interest

The author declares that there are no conflicts of interests of this paper.

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