Normal Tension Glaucoma - a Sick Eye in a Sick Body

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For centuries, glaucoma is being recognised as an irreversible optic neuropathy as a result of damages caused by an elevated intraocular pressure (IOP). Nowadays, however, we know that glaucoma occurs in patients with IOP entirely in the "normal" range (typically taken as less than 21 mmHg). For this group of glaucomas, termed as Normal Tension Glaucoma (NTG), numerous studies have demonstrated that factors other than IOP may play a role in its pathogenesis. Many of these factors are general medical diseases and hence, NTG can be of interest to our general practitioner audience. In fact, Felix Lagrange of Bordeaux was the first to note that glaucomatous optic neuropathy (GON) may in fact be a "sick eye in a sick body" as early as in 1922.

Role of Blood Pressure

Kummell in 1911 was one of the first to describe the relationship between high blood pressure (BP) and glaucoma. Thereafter, numerous studies demonstrated the correlation between arterial hypertension and glaucoma as well as between arterial hypotension and glaucoma. Patients with NTG or primary open angle glaucomas were shown to be more likely to suffer from hypertension than normal controls. We know that the relationship between hypertension and mean ocular perfusion pressure is not straightforward and simple hypertension does not lower the mean ocular perfusion pressure. In fact, assuming the same vascular tone and intact autoregulatory mechanism, a modest increase in BP may increase the ocular perfusion pressure a bit. The treatment of hypertension, however, has been shown to be the culprit in resulting NTG and optic nerve ischaemic damages. Hayreh and co-workers performed an important work in 24-hour ambulatory BP monitoring to look for possibility of a nocturnal dip (>20% from baseline is considered as large dippers). In case such a dip exists, a close liaison with our fellow physicians may be justified to fine tune to BP control to avoid the optic nerve "dying in the night".

Role of Vasospasm

Vascular dysregulation, such as inappropriate constriction or insufficient dilatation in the microcirculation to stimuli such as coldness, has been proposed as a risk factor for glaucoma. Studies have shown that patients with NTG had reduction of nial-fold capillary blood-flow velocity upon cold provocation, significantly more so than other open angle glaucomas and normal subjects. A number of endothelium-derived vasoactive substances maintain and modulate the vascular tone throughout the body and the eye. In the ophthalmic vascular bed, a constant basal release of nitric oxide (NO) maintains the circulation in constant vasodilatation, whereas endothelin-1 (ET-1) was shown to cause marked vasoconstriction. Imbalance of the level of these agents, possibly in concert with various other vasoactive substances, was postulated as one of the models for pathogenesis leading to optic nerve damage. The role of treatment with Calcium-channel blockers in this respect is uncertain. On the other hand, the use of the Chinese herbs Gingko Biloba Extract showed initial beneficial evidence though of course much more studies will be needed.

Role of Migraine

Functional vasospasm of the brain vessels is linked to the pathogenesis of migraine. In fact, both NTG and migraine are associated with systemic vascular dysregulation. Phelps and Corbett found a higher prevalence of migraine-like headaches in NTG, compared to other open angle glaucomas and normal controls. These findings were supported by data from...
Role of Sleep Apnoea Syndrome (SAS)

Walsh and Montplaisier were among the first who reported a combination of familial glaucoma and sleep apnoea syndrome across two generations of a family. Later studies suggested a significant association between SAS and incidence of NTG and open angle glaucoma. Respiratory Disturbance Index (RDI) during night sleep correlated with visual field loss variance and benefit to the NTG as well. Impaired perfusion to the optic nerve head due to SAS, NTG, analysed the risk factors for progression in the Tension Glaucoma Study, one of the largest studies on glaucoma patient showing a typical "nocturnal dip" in blood pressure. Sleep apnea syndrome is associated with sleep apnea syndrome. Later studies suggested a significant association between sleep apnea syndrome.

Role of Silent Cerebral Infarcts (SCI)

Stroman and coworkers performed Magnetic Resonance Imaging (MRI) in NTG subjects and found significantly more diffuse cerebral small-vessel ischaemic changes when compared to controls. Later studies indicated that the prevalence of ischaemic MRI changes can be found in as much as 34% of NTG patients. It has been proposed that these findings may reflect a vascular cause in some NTG patients, possibly related to cerebral small-vessel ischaemia. Further studies are warranted. Meanwhile, we do not recommend a routine neuroimaging for patients with NTG. However, in case neuroimaging is done for NTG to rule out any "space occupying lesion" along the visual pathway as a potential cause of visual field defect at hand, we recommend to actively look for the presence of cerebral ischaemic changes, or silent cerebral infarcts (SCI). As SCI is a potent independent risk factor for future stroke, liaison with neurologists may be indicated for stroke prophylaxis.

References


Messages: NTG is a Sick Eye in a Sick Body

Vascular factors may play a role in pathogenesis. Therefore, 1. look for arterial hypertension and hypotension. Consider 24-hour ambulatory BP measurement and avoid nocturnal arterial hypotension. 2. look for vasospasm (e.g. Raynaud’s phenomenon) 3. look for migraine, consider liaison with neurologists for treatment 4. look for Sleep Apnoea Syndrome, consider liaison with specialists for treatment 5. look for Silent Cerebral Infarcts, consider liaison with neurologists for stroke prophylaxis.