Glaucoma Under Pressure: IOP, BP, OPP, and ICP

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Pathophysiology of Glaucoma: Initial Insult

ISCHAEMIC Stress

VASCULAR FACTORS

BIOMECHANICAL Stress

NTG

IOP

POAG

Lamina Cribrosa

Scanning EMs of human optic nerve head following partial enzymatic digestion


Optic Nerve Head

Schematic representation of blood supply of:
(A) the optic nerve head (Hayreh 1978); (B) the optic nerve (Hayreh, S.S. 1974).

Abbreviations: A = arachnoid; C = choroid; CRA = central retinal artery; Col. Br. = Collateral branches; CRV = central retinal vein; D = dura; LC = lamina cribrosa; NFL = surface nerve fiber layer of the disc; OD = optic disc; ON = optic nerve; P = pia; PCA = posterior ciliary artery; PLR and PRL = prelaminar region; P = pia; RA = retinal arteriole; R = retina; SAS = subarachnoid space.
Overview:

To compare brimonidine to timolol maleate in preserving visual function in low-pressure glaucoma

- Randomized, double-masked, multicenter clinical trial

**Outcome**

- “While low-pressure glaucoma patients treated with brimonidine was protective compared to timolol, mean ocular perfusion pressure increased the risk of VF progression.”

- AJO 2012

There are several factors potentially reducing the OBF. The vascular dysregulation is one of the main mechanisms invoked. It is defined as the inability of a tissue to maintain a constant blood supply despite changes in perfusion pressure secondary to vascular abnormalities or to the role of local vasospastic/vasodilating agents.

Also the blood pressure has a predominant role: several studies reported that low blood pressure was a significant risk factor for visual field defect progression in NTG (Leighton and Phillips, 1972; Okumura et al., 2012). However, the real association between these findings is still debated.

In a recent study in patients with NTG, Abegao Pinto et al. (2012) reported the reduction of blood flow velocities in retrobulbar arteries and in cerebral circulation. They found that, while in healthy individuals there was a linear correlation between vascular pulsatility index and resistive index, this relation was not present in NTG patients.

Su et al. (2006, 2008), using the brachial artery ultrasound assessment of endothelium-dependent flow-mediated vasodilation, provided evidence of a generalized endothelial dysfunction in patients with NTG.

The vascular dysregulation in NTG was also related to alterations of local agents. Henry et al. (1999, 2006) documented an altered vascular reactivity to endothelial vascular dysregulation factors. This should be intended as expression of an impairment of the peripheral endothelium-mediated vasodilatation.

Buckley et al. (2002) analyzed cutaneous artery biopsies showing a selective defect in the agonist-mediated release of endothelium-derived vasodilators. These findings support the...
Habitual IOP and Pulse Pressure

24 Hour IOP (and BP)

Example of 24-hour IOP Recording Curve: Healthy Subject

How Does It Work?

- The monitoring tool, embedded in a soft silicone contact lens, includes an integrated micro-mechanical sensor powered remotely by telemetry.

- The information is then stored in a portable recorder.

- Characteristics:
  - Diameter: 14.1 mm
  - Base Curves: 8.4 (STEEP); 8.7 (MEDIUM); and 9.0 (FLAT)
  - Lens material: Silicon

- For glaucoma patients
- Patients with a risk of glaucoma
- Patients with a suspicion of high IOP

- Continuous monitoring during night & day
- Personalized diagnosis
- Better disease management
- Adapt treatment to changing condition
Habitual IOP and Pulse Pressure

Ocular Perfusion Pressure

\[ MOPP = \frac{2}{3} MAP - IOP \]
\[ MAP = DBP - (SBP - DBP) \]
\[ SPP = SBP - IOP \]
\[ DPP = DBP - IOP \]
Observations on Degenerative Changes Within the Optic Nerve in Patients With Primary Open Glaucoma and Arterial Hypertension: 6-Month Follow-Up
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Purpose: To determine the effect of the time of hypotensive drug administration on the progress of degenerative changes within the optic nerve in patients with hypertension and glaucoma.

Sample: Two groups were included in the study:
- Group A: Dippers taking drugs in the mornings
- Group B: Non-dippers taking drugs both mornings and evenings.

Results: After 6 months, Group B showed significant drop in nocturnal DBP (Month 1 = 73.27 vs Month 6 = 67.50 mmHg), nocturnal mean BP (89.34 vs 84.65 mmHg), min. DBP (50.74 vs 44.03 mmHg), nocturnal OPP (43.0 vs 39.73 mmHg), RNFL thickness (131.31 vs 113.12 µm), and retinal blood flow.

Conclusion: Taking hypotensive drugs in the evening may significantly decrease retinal blood flow, cause degenerative changes within the optic nerves, and result in greater loss in the field of vision.
Investigation of Cerebrospinal Fluid Pressure and Optic Nerve Head Structural Changes in Glaucoma

Introduction

Recent experimental and clinical studies have reported that cerebrospinal fluid pressure (CSFP) is strongly associated with low-teen IOP or high-teen IOP normal-tension glaucoma (NTG) patients. To investigate the association between estimated trans-lamina cribrosa pressure difference (TLCPD) and prevalence of NTG with low-teen and high-teen IOP, we estimated CSFP and calculated TLCPD using a formula published previously by Xie et al. (2015). Since measurement of CSFP requires an invasive procedure, we estimated based on a population-based study design. Additionally, we further sought possible associations between systemic vascular parameters and TLCPD.

Materials and Methods

This study was supported by the World Health Organization (WHO) Collaborating Centre for Prevention of Blindness in Asia and the Pacific. The study was conducted in the cities of Seoul and Busan, South Korea, and the study population included patients from the community and hospital-based settings.

Conclusion

Low CSF pressure likely associated with NTG.

Cerebrospinal Fluid Pressure

Clinical studies reported that patients with NTG had significantly lower CSF pressure and a higher trans-lamina cribrosa pressure difference (TLCPD) and prevalence of NTG with low-teen and high-teen IOP. To investigate the association between estimated trans-lamina cribrosa pressure difference and prevalence of NTG, we estimated CSFP using a previously developed formula, cerebrospinal fluid pressure (CSFP) in mmHg was estimated from its Institutional Review Board and survey conducted by the Korea Centers for Disease Control and Prevention with approval from the Institutional Review Board.

Study population

The study included patients from the community and hospital-based settings in the cities of Seoul and Busan, South Korea. The study population consisted of patients with low-teen IOP and high-teen IOP NTG.

Conclusions

The prevalence of NTG in the low-teen IOP group (p = 0.395; 2.31 ± 0.18 mmHg) was significantly lower compared to the high-teen IOP group. On the other hand, there was no significant difference in TLCPD between normal and low-teen IOP subjects, in whom hypertension may be more closely associated. This study suggests that the underlying mechanism may differ between low-teen and high-teen NTG patients.

New Pressure Model of Glaucoma

This model could explain why patients with NTG tend to have a low systemic BP, and why eyes with normal IOP glaucoma and eyes with high-pressure glaucoma, in contrast to eyes with a direct vascular optic neuropathy, show profound similarities in the appearance of the ONH.
Cerebral Spinal Fluid Pressure

**What do we know?**

- Trans-scleral pressure difference
- Low CSF pressure associated with NTG – possibly higher-teen NTG
- Finally provides a reasonable explanation for aspects of NTG
- Implication for venous outflow