Management of isolated ocular hypertonia

Written with the assistance of Florent Aptel, Antoine Bastelica, Hélène Bresson-Dumont, Nathalie Collignon, Philippe Denis, Jean-Philippe Nordmann

1. CONTEXT

Isolated ocular hypertonia is defined by an intraocular pressure (IOP) greater than 21 mmHg in a patient with open iridocorneal angle without glaucomatous alteration of the optic nerve head and characteristic impairment of the visual field.

The pathological raise in IOP is the major **risk factor for conversion to primary open-angle glaucoma** (POAG) and a critical factor **in the progression of** glaucoma. The overall risk for converting to glaucoma is estimated at **about 10% at 5 years**. Most patients with ocular hypertonia (OHT) are not at risk for glaucoma and in 30-40% of untreated patients, the risk of developing the disease is less than 1% each year.

It is therefore important to identify patients who require a treatment because lowering IOP decreases the overall risk of developing glaucoma. This risk increases exponentially with the IOP level. High OHT (>28-30 mmHg) could be associated with a risk **of retinal vein occlusion**.

2. DEFINITION - EPIDEMIOLOGY

The threshold of hypertonia is arbitrarily set at 21 mmHg and its diagnosis is made from **repeated measurements** of the IOP. Due to its diurnal variations, the finding of an IOP greater than 21 mmHg should be confirmed **several times** prior to confirm the diagnosis. The IOP is physiologically raised with age, which explains the **increased prevalence of OHT with age**. About 2% of the population over the age of 40 and almost 10% of the population over 70 years have OHT[1]. It is also higher in black subjects and patients with myopia, diabetes, hypertension.

3. MEASURING THE INTRAOCULAR PRESSURE

Measuring the IOP by Goldmann applanation tonometry remains the **reference technique**. If an airpuff tonometer (non-contact tonometry) is used, comparative measurements should be made to calibrate the device and the Goldmann tonometer should be used to verify any up and down abnormal measurement. The **tonometers** operating according to a principle other than applanation (Pascal, ORA, rebound tonometry…) could give **more realistic results**, but are currently not an

[1] *Leske MC. The epidemiology of open-angle glaucoma: a review. Am J Epidemiol 1983; 118: 183-91.*

alternative to Goldmann tonometry.

The IOP should be measured **before performing gonioscopy or any pupil dilation**. Because of diurnal variations, **the measurement time** should be mentioned. The **diurnal curves** of the IOP (or "mini-curves" made during the day for convenience with 3-5 measurements) may provide useful information on the existence of pressure peaks. When repeated measurements of the IOP are not possible the same day, it is possible to schedule the subsequent consultations of the patient at different times, which grossly allows understanding IOP stability.

The quality of the measurement of the IOP with the Goldmann tonometer is related to the consideration of intrinsic (patient-related) and extrinsic factors that may alter the tonometry.

CAUSES OF IOP OVERESTIMATION:	CAUSES OF IOP UNDERESTIMATION:
thick cornea	**thin cornea**
fluorescein excess	**fluorescein insufficiency**
tearing	**dry eye**
prolonged apnea	**prolonged accommodation**
tight shirt collar	**insufficient illumination of the cone**
off-center cone	**cone-eyelid contact**
cone-eyelid or eyelashe contact	**blinking**
blepharospasm	**with-the-rule astigmatism** (especially if >3 diopters)
against-the-rule astigmatism (especially if >3 diopters)	**repeated measurements of the IOP**

4. MEASURING THE CENTRAL CORNEAL THICKNESS

Corneal pachymetry is an **essential examination** when faced with any isolated OHT **because the central corneal thickness** (CCT, mean value of 540 ± 30 µm) changes the measurement of the IOP by tonometry. Thus, the thin corneas result in an underestimated measurement while the thick corneas (more than 600 microns) typically overestimate the IOP. Conversely, patients with isolated OHT frequently have a thick cornea[2].

Ultrasonic pachymetry is the reference technique, but the other "non-contact" techniques (Orbscan, specular microscope) also provide reliable and reproducible measurements. There are no charts to correct the IOP values based on corneal pachymetry and the proposed nomograms are all **approximate, in particular after refractive surgery**. In daily practice, it however appears that a thickening of 100 µm compared to the normal CCT leads to an overestimation of the IOP of about 5 mmHg[3]. There is no need to repeat pachymetry at each consultation because the CCT is relatively stable over time.

[2] *Argus WA. Ocular hypertension and central corneal thickness. Ophthalmology 1995; 102: 1810-2.*
[3] *Doughty MZ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. Surv Ophthalmol 2000; 44: 367-408.*

5. CONDUCT OF THE OPHTHALMOLOGICAL EXAMINATION

- **QUESTIONING**

The questioning investigates the ocular, personal and family **history** of the patient, and the **treatments** received (**corticosteroids** with an iatrogenic risk of hypertonia or drugs with a mydriatic effect, concept of drug intolerance) and the risk factors for POAG. **Some of these risk factors** may be known from patient questioning**: age, family history of glaucoma, ethnic origin (black).** Other factors are also involved such as the daily fluctuations in IOP, diabetes (discussed role), myopia, low and high blood pressure.

- **PHYSICAL EXAMINATION**

The physical examination includes the **measurement of the visual acuity** (near and distance) before and after optical correction to investigate the presence of ametropia (myopia, hyperopia), **slit-lamp biomicroscopy** of the anterior segment and iridocorneal angle (gonioscopy before pupil dilation), measurement of the IOP and ECC, analysis of the optic nerve head and peripapillary retinal nerve fiber layer and the reading of the visual field. The examination is bilateral and comparative.

- ✓ ***Anterior segment:*** *investigate the presence of signs suggestive of a secondary cause of OHT: capsular pseudoexfoliation, pigment dispersion, iris and angle neovascularization, iris or angle tumor, ocular inflammation, pupil deformation (pupil reactivity). The anterior chamber depth should be estimated in the center and periphery.*

- ✓ ***Measurement of the IOP:*** *tonometry before pupil dilation and before focus lens implantation on the eye. The measurement time should be noted in the record.*

- ✓ ***Measurement of the ECC****: the record should include a pachymetric measurement of the ECC.*

- ✓ ***Gonioscopy****: gonioscopy investigates the presence of signs* ***suggestive of iridocorneal angle closure*** *(degree of angle opening by accurate identification of angle structures in the 4 quadrants, areas of iris apposition, iridocorneal synechia) or a* ***cause of secondary OHT*** *(angle recession, pigment dispersion, iridocorneal synechiae, angle neovascularization, inflammatory precipitates on the trabecular meshwork).*

- ✓ ***Examination of the optic nerve head and peripapillary retinal nerve fiber layer****: the most suitable technique is stereoscopic biomicroscopy, usually through a dilated pupil. Examining the optic nerve head is always necessary, even when pupil dilation is contraindicated. A direct ophthalmoscopic examination may be used, because it allows increasing the image size and therefore enables good visualization of the optic disc details. A red-free light with a blue filter (490 nm) is recommended for examining the peripapillary retinal nerve fiber layer.* ***Pictures*** *(at best, stereophotographic)* ***of optic discs and peripapillary retinal nerve fiber***

layer *are useful for the early detection of the first signs and to have a reference examination.* ***Biomicroscopy of the optic nerve head*** *should investigate, after measurement of the optic disc size, an initial damage at the neuroretinal ring and peripapillary retinal nerve fiber layer (localized or diffuse deficits of the retinal nerve fiber layer, width and color of the neuroretinal ring, size and depth of the cupping of the optic disc, vertical and horizontal cup/disc ratios, pallor-cupping dissociation, position of the circumlinear vessel, presence of optic disc hemorrhages, peripapillary atrophy)*[4].

- **AUTOMATED EXAMINATION OF THE OPTIC NERVE HEAD AND RETINAL NERVE FIBER LAYER**

At the stage of hypertonia, the physical examination may be completed by a **morphometric analysis of the optic nerve head** (optical coherence tomography OCT, but also HRT2 confocal microscopy) or retinal nerve fiber layer (HRT2, OCT-3, GdX)[5],[6],[7],[8]. Optic disc imaging devices provide morphometric values (surfaces and volumes of the optic disc structures, thickness of the retinal nerve fiber layer) for accurate monitoring. The characteristic image showing the double-humped shape of the retinal nerve fiber layer in normal subjects is due to the greater density of retinal nerve fibers in the upper and lower area and at the bottom. In patients with glaucoma, the hump elevations are less pronounced and may even disappear in advanced cases. The macular ganglion cell complex may also be studied through specific OCT programs, and its impairment would be an early marker of glaucomatous optic neuropathy. The **accuracy** of optic disc imaging devices is poorer in eyes with high myopia or congenital optic disc defects. For each of these automated analyzers, the line between the normal (isolated OHT) and the pathology (early glaucoma) is not always unequivocally defined. The **comparison with the other parameters** (IOP, optic disc, visual field, background) **remains essential**.

- **PERIMETRY TEST**

Analyzing the central visual field using a preliminary strategy by **standard** ("white-white") **automated perimetry** is recommended to detect the first signs of early functional impairment. The choice of the program is at the physician's discretion, but generally includes the exploration of the central 24° or 30°. Some algorithms (Fastpac™, SITA, TOP Strategy) allowing a reproducible and rapid analysis of the visual field may also be used. When performing automated perimetry is not possible, the Goldmann kinetic perimetry is an acceptable but less reliable alternative. Particular attention should be paid to the reliability indices obtained by perimetry. It is preferable to monitor

[4] *Renard JP, et coll. Bilan en pratique. L'hypertonie oculaire isolée. J Fr Ophtalmol 2005; S13-S6.*
[5] *Tjon-Fo-Sang MJ, de Vries J, Lemij HG. Measurement by nerve fiber analyzer of retinal nerve fiber layer thickness in normal subjects and patients with ocular hypertension. Am J Ophthalmol 1996; 122: 220-7.*
[6] *Kothy P, Vargha P, Hollo G. Glaucoma-screening with the Heidelberg Retina Tomograph II. Klin Monatsbl Augenheilkd 2003; 220:540-4.*
[7] *Reus NJ, Colen TP, Lemij HG. Visualization of localized retinal nerve fiber layer defects with the GDx with individualized and with fixed compensation of anterior segment birefringence. Ophthalmology 2003; 110: 1512-6.*
[8] *Ford BA, et coll. Comparison of data analysis tools for detection of glaucoma with the Heidelberg Retina Tomograph. Ophthalmology 2003; 110: 1145-50.*

patients using the same test, and a monitoring interval of 12-24 months may be proposed if the initial visual field is normal.

The anatomical alterations of the optic nerve usually but not systematically **precede the glaucomatous visual field disturbances** at the early stage[9]. There is a pivotal point where the visual field is normal while the cupping of the optic disc already shows the characteristic signs of glaucomatous damage. In these cases, **short-wavelength** (blue-yellow) **perimetry** or FDT (Frequency Doubling Technique) perimetry may detect visual field defects before standard perimetry[10]. **Combining these examinations** could increase the sensitivity of the diagnosis of glaucoma.

6. DIFFERENTIAL DIAGNOSIS

- **DEPENDING ON THE ASPECT OF THE IRIDOCORNEAL ANGLE**

When the iridocorneal angle is open, the main differential diagnosis is **primary open-angle glaucoma in its early stage**. The diagnosis should be based on a careful examination of the optic nerve head, and the analysis of the visual field reading. The IOP alone is therefore insufficient to define glaucoma. Indeed, several studies have demonstrated that one out of two glaucoma patients permanently has IOPs <22 mmHg[11].

When the iridocorneal angle is narrow, a partial or permanent angle closure (primary angle closure or plateau iris configuration) should be considered. The causes of secondary angle closure (chronic uveitis, angle trauma, rubeosis iridis…) should also be discussed.

- **DEPENDING ON THE ETHIOLOGY**

The causes **of secondary OHT** should be discussed: search for cortisone impregnation, capsular pseudoexfoliation, pigment dispersion syndrome, angle neovascularization, trabecular inflammation, angle recession or cyclodialysis.

7. CLINICAL MONITORING

The frequency of examinations should be adapted to the age of the patient, the IOP level and the existence of **risk factors for glaucoma**. **These risk factors** include**: age, family history of glaucoma, ethnic origin (black), reduced CCT**. Other factors are also involved such as the daily fluctuations in IOP, diabetes (discussed role), myopia, low and high blood pressure. The presence of capsular pseudoexfoliation or pigment dispersion syndrome also results in a greater variability in IOP, and therefore increases the risk for conversion to glaucoma.

An interval of 6-24 months between two consultations may be proposed, based on the above-mentioned criteria, but may be shorter, in particular when a treatment is prescribed (assessment of the efficacy and safety of the drug) or when optic disc or visual field changes are present. Perimetry

[9] *Harwerth RS, et coll. Ganglion cell losses underlying visual field defects from experimental glaucoma. Invest Ophthalmol Vis Sci 1999; 40: 2242-50.*
[10] *Landers JA, Goldberg I, Graham SL. Detection of early visual field loss in glaucoma using frequency-doubling perimetry and short-wavelength automated perimetry. Arch Ophthalmol 2003; 121: 1705-10.*
[11] *Leske MC, Heilj A, Hussein M. Factors for glaucoma progression and the effect of treatment: the Early Manifest Glaucoma Trial. Arch Ophthalmol 2003; 121: 48-56.*

or an automated examination of the optic nerve head and retinal nerve fibers is not systematically performed at each consultation.

8. THERAPEUTIC MANAGEMENT

- **Distinction between isolated OHT and early glaucoma**

While there is a **consensus** to treat as soon as early visual field damage or optic disc signs suggestive of glaucoma are present, the therapeutic decision in isolated OHT is more discussed. **OHT and early glaucoma** are difficult to distinguish and the line between the normal and the pathology is relatively imprecise, fluctuating depending on the screening technique used. This distinction is yet a critical issue because early glaucoma deserves treatment while a raised PIO may just be monitored. The "OHT = glaucoma" equation leads to treat a large number of patients, without distinction and with the risk of burdensome, poorly tolerated treatment that may be costly for the community.

- **Ocular Hypertension Treatment Study (OHTS)**

The OHTS has provided essential information on the clinical characteristics of patients with hypertonia and the natural evolution of OHT. The aim of this study was to assess the risk of progression of OHT to glaucoma (defined by the existence of reproducible visual field and optic disc damages)[12]. The results show that **90% of patients with raised IOP do not develop glaucoma after five years,** the treatment (20% lowering in IOP from baseline) **reduces the risk by about 50%**.

Several risk factors for conversion have been highlighted in the OHTS: age, horizontal and vertical cup/disc ratios, localized deviation on perimetry (PSD), thin cornea). A similar European study (the European Glaucoma Prevention Study) has also evidenced the same risk factors than the OHTS[13](with the addition of the cup/disc ratio asymmetry). These two studies show that **measuring the central corneal thickness is essential during the examination of any OHT**, a relatively large number of patients with hypertonia no longer have hypertonia considering the ECC, and most patients with raised IOP do not develop glaucoma. The extension of patient follow-up in the OHTS indicates that a delayed treatment of OHT is possible if the risk for conversion to glaucoma is low, but it is advised to treat early if it is high[14].

9. CONCLUSION - SUMMARY

- The finding of an IOP greater than 21 mmHg should be confirmed several times because the IOP is a variable parameter, undergoing physiological, postural, diurnal or seasonal

[12] *Kass MA, et coll. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol 2002; 120: 701-13.*
[13] *European Glaucoma Prevention Study (EGPS) Group. Predictive factors for open-angle glaucoma among patients with ocular hypertension in the European Glaucoma Prevention Study. Ophthalmology 2007; 114: 3-9.*
[14] *Kass MA, et coll Ocular Hypertension Treatment Study Group. Delaying treatment of ocular hypertension: the ocular hypertension treatmentstudy. Arch Ophthalmol. 2010;128:276-87.*

changes.

- The Goldmann tonometer is the reference device for measuring the IOP but the use of an airpuff or "non-contact" tonometer is possible. A raised IOP measured with an airpuff tonometer should be verified with a Goldmann tonometer. A single measurement of the IOP is inadequate to detect glaucoma in its early stage.

- Measuring the central corneal thickness is an essential examination in OHT due to changes in IOP measurement induced by the corneal thickness. There is no need to repeat corneal pachymetry measurements at each consultation because the CCT is relatively stable over time.

- The ophthalmologic examination should definitely include the careful analysis of the optic disc and peripapillary retinal nerve fiber layer, and a thorough assessment of the visual function using fine techniques such as blue-yellow or FDT perimetry. The optic nerve and/or peripapillary retinal nerve fiber layer damage generally precedes that of the visual field.

- Gonioscopy should be systematically performed to rule out a narrow angle or a secondary cause, including pigment dispersion or pseudoexfoliation.

- No systematic approach should be adopted and the decision to treat or not should be taken on a case-by-case basis, depending on the IOP and associated risk factors and the degree of acceptance of a treatment.

- Patient information should be preferred, to make him understand the importance of a regular monitoring but also to make him accept a prophylactic treatment for many years.