Ocular Hypertension

a) Define ocular hypertension. b) Investigations and management of a case of ocular hypertension. [2+ (4+4)] J2015

Definition

- **Ocular hypertension** is defined as a condition in which IOP is elevated above an arbitrary cutoff value, typically 21 mm Hg, in the absence of
  - Optic nerve, retinal nerve fiber layer, or visual field abnormalities,
  - Ocular or systemic disorder contributing to the rise in IOP.
  - Closed angles on gonioscopy (open angles)

- Estimates of the prevalence of ocular hypertension in the United States vary considerably and may be as high as 8 times that of diagnosed POAG.

- Distinguishing between ocular hypertension and early POAG is often difficult.

- The ophthalmologist must look carefully for signs of early damage to the optic nerve, such as
  - Focal notching,
  - Asymmetry of cupping,
  - Optic disc hemorrhage,
  - Nerve fiber layer defects,
  - Or subtle visual Field defects.

- **Glaucoma suspect**- A patient may be considered a POAG suspect (i.e., more likely to develop glaucoma than the average person) on the basis of
  - Family history of the disease,
  - Suspicious-appearing optic disc, or nerve fiber layer appearance in the absence of a visual field defect;
  - Or a visual field defect suggestive of glaucoma in the absence of a corresponding glaucomatous optic nerve abnormality.
  - Or an elevated IOP.

- An individual who has a first-degree relative with POAG has approximately an eight-fold greater risk of developing the disease.

- Prudence dictates that anyone with a first-degree relative (parent, sibling, or child) with POAG should have regular ocular examinations, including tonometry and ophthalmoscopy, every 1 or 2 years up to age 60, with increasing frequency over age 60.

- Researchers have identified
  - Elevated IOP,
  - Optic disc abnormalities,
  - Increasing age,
  - Family history of glaucoma,
  - Decreased outflow facility,
  - And systemic vascular diseases as the factors that best predict the development of POAG.
The use of frequency-doubling technology and pattern may be useful for detecting early loss of visual function. If signs of optic nerve damage are present, the diagnosis of early POAG and initiation of treatment should be considered.

**Risk Factors in ocular hypertension**

<table>
<thead>
<tr>
<th><strong>Prospectively proven risk factors</strong></th>
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<tbody>
<tr>
<td>1. Thin corneas (&lt;535 microns)</td>
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<td>2. Elevated intraocular pressures</td>
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<td>3. Increasing age</td>
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<td>4. Vertical cupping of the optic nerve (&gt;0.6)</td>
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<td>5. Increased pattern standard deviation on threshold perimetry</td>
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<td>6. Abnormalities in the optic nerve with the scanning laser ophthalmoscope</td>
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<td>7. Pseudoexfoliation</td>
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**Putative risk factors**

1. **Socio-demographic factors**
   - Gender (women)
   - Race (blacks and Hispanics)

2. **First-degree relative with open-angle glaucoma**

3. **General medical status**
   - Cardiovascular disease
     - Coronary artery disease
     - Atherosclerosis
     - Cerebrovascular disease
     - Peripheral vascular disease
   - Abnormal cold pressor test
   - Hypertension
   - Aggressive antihypertensive therapy
   - Hypotension
   - Hemodynamic crisis

   - Endocrine disease
     - Thyroid disease
     - Diabetes (some studies say a risk, others a protective factor)
     - Acromegaly
     - Cushing disease

4. **Aqueous humor dynamics**
   - Large diurnal variation in IOP
   - Rising IOP with time
   - Increased IOP in supine position

5. **Optic disc**
   - Large cup-to-disc diameter ratio
   - Optic disc hemorrhage
   - Filling defects on fluorescein angiography
   - Parapapillary atrophy

6. **Miscellaneous ocular findings**
   - Myopia
   - Pigment dispersion
   - Central retinal vein occlusion
Epidemiology
- The prevalence of ocular hypertension varies in different ethnic groups.
- Its prevalence increases with age.
- Highest prevalence of 12.6% was reported amongst Afro-Caribbean population in one study.
- In the Framingham Eye Study conducted in Whites, its prevalence was 6.2% amongst under 65 age group, while 8.7% in individuals above 75 years of age.
- In southern India prevalence of 1.1% in individuals above 40 years of age has been reported.

Diagnosis
- Ocular hyperstension is a diagnosis of exclusion.
- History of ocular trauma and steroid use should be ruled out.

Investigations
1. An ocular hypertensive individual requires **periodic examinations**, including
   - Tonometry,
   - Perimetry,
   - Optic disc assessment.
   - Frequency-doubled perimetry may be helpful in identifying the earliest glaucomatous visual field defects, although these techniques may have a more significant noise level that reduces specificity.
   - Blue-yellow perimetry/ Frequency-doubled perimetry may be helpful in identifying the earliest glaucomatous visual field defects, although these techniques may have a more significant noise level that reduces specificity.
   - Stereoscopic optic disc photographs provide baseline information against which one can determine changes in the optic nerve over time.
   - Nerve fiber layer photographs may also be useful.
   - Ocular coherence tomography,
   - Confocal scanning laser ophthalmoscopy
   - Scanning laser polarimetry
   - Short-wavelength automated perimetry

2. (vii-x) are **Newer modalities** such appear to be able to detect optic nerve functional damage and anatomic damage before they are seen with clinical examination or with standard threshold static.

3. **Other tests** that have shown in longitudinal studies to predict those who have already developed early glaucoma or who will develop it in the future include
   - Blue-yellow perimetry
   - Motion detection perimetry
   - Pattern electroretinogram,
   - Optic nerve changes by scanning laser ophthalmoscopy- Nerve fiber layer assessment by scanning laser polarimetry shows reduced nerve fiber layer levels in ocular hypertensive patients compared with normal.

4. **Nerve fiber layer defects** have been shown to precede visual field defects in ocular hypertensive eyes converting to open-angle glaucoma by as much as 4–5 years.

5. **Fluorescein angiographic filling defects** in the optic nerve may precede development of visual field loss in ocular hypertensive patients.

6. **Parapapillary atrophy**, as well as larger vertical cup-to-disc ratio, and small neural retinal rim area-to-disc area ratio were associated with progression. An enlarging area of parapapillary atrophy was also correlated with development of glaucoma.

7. **STARRII Risk Calculator**
   - Using the OHTS results, Medeiros and colleagues have developed a risk calculator for ocular hypertensives that can be helpful in predicting the relative risk for actual glaucoma development.
They have validated this model in a prospective study independent of the OHTS group of patients.

A scoring tool based on this model has been published by Pfizer Corporation (STARRII Risk Calculator) and, as of this writing, has been provided to ophthalmologists and others free of charge.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
<th>Example</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>30-80</td>
<td>72</td>
</tr>
<tr>
<td>IOP (mm of Hg)</td>
<td>20-32</td>
<td>29</td>
</tr>
<tr>
<td>CCT (micrometer)</td>
<td>475-650</td>
<td>501</td>
</tr>
<tr>
<td>PSD (dB)</td>
<td>0.50-3.00</td>
<td>1.75</td>
</tr>
<tr>
<td>C/D</td>
<td>0.00-0.80</td>
<td>0.70</td>
</tr>
<tr>
<td>Probability of conversion in 5 years</td>
<td>%</td>
<td>67.1%</td>
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**Treatment**

- Only 1-2% patients progressed to POAG in a yearly follow-up in OHTS trial.
- Considering the low rate of progression to POAG, cost of ocular hypotensive medications, long term compliance issues and side effect of drugs, not every case of ocular hypertension is subjected to treatment with ocular hypotensives.
- Therefore, treatment is recommended only in high risk group.
- Lowering of IOP by at least 20% is recommended.
- Topical beta blockers or prostaglandin analogues are usually the preferred agents.
- Patients with moderate risk of progression should be monitored closely and treatment is initiated with the earliest sign of glaucomatous damage.
- While once in a 2 year follow-up is recommended for low risk individuals.
- Suggested risk criteria for progression to POAG is described below.

<table>
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<tr>
<th>High risk</th>
<th>Moderate risk</th>
<th>Low risk</th>
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<tbody>
<tr>
<td>Requires treatment. Aim for at least 20% IOP reduction.</td>
<td>Annual follow-up. Treatment initiated at the earliest documented glaucomatous damage.</td>
<td>Follow-up every 2 years.</td>
</tr>
<tr>
<td>1. Retinal nerve fiber layer defects.</td>
<td>1. IOP 24-29 mmHg without retinal nerve fiber layer damage.</td>
<td>1. IOP 22-23 mmHg with central corneal thickness more than 588 microns.</td>
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<tr>
<td>2. Parapapillary changes.</td>
<td>2. IOP 22-25 mmHg with central corneal thickness &lt;555 microns.</td>
<td>2. Vertical cup-disc ratio 0.4 or more with central corneal thickness more than 588 microns.</td>
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<tr>
<td>3. IOP &gt; 30 mmHg</td>
<td>3. Vertical cup-disc ratio 0.4:1 or more with central corneal thickness between 555-588 microns.</td>
<td>3. Family history of POAG in first degree relative.</td>
</tr>
<tr>
<td>4. IOP &gt; 26 mmHg with central corneal thickness &lt;555 microns.</td>
<td>4. High Myopia.</td>
<td>4. Vertical cup-disc ratio 0.4 or more with central corneal thickness more than 588 microns.</td>
</tr>
<tr>
<td>5. Vertical cup-disc ratio 0.4:1 or more with central corneal thickness &lt;555 microns.</td>
<td></td>
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</table>

1. Debate has been sharpened by recent studies showing that ocular hypertensive patients can lose
   - 40% or even 50% of their optic nerve axons despite having normal kinetic visual fields,
   - 35% of their ganglion cells despite normal automated threshold perimetry.
Despite this finding, the current recommendation is that most ocular hypertensive individuals do not require medical therapy.

Treatment should be reserved for those patients who demonstrate early damage and for those who are thought to be at high risk for developing glaucoma (see below).

2. **Therapy should be instituted** if early damage is detected or if the patient appears to be at high risk for developing POAG based on the risk factors identified above.

   ✓ Many clinicians institute medical treatments if the IOP is 30mmHg or greater, noting that the prevalence of glaucoma at this pressure level is 11–29%

   ✓ It may also be appropriate to recommend therapy for individuals with IOPs in the middle-to-upper 20s who also have one or more risk factors

   ✓ Following are other possible indications for treatment:

   i. **A one-eyed patient.** Many clinicians are more aggressive in treating one-eyed patients.

   ii. **A young patient.** Some ophthalmologists prescribe medical treatment more rapidly for young patients who will be exposed to high pressure for many years. This may be questionable reasoning because, often, young optic nerves are more resistant to the effects of elevated IOP than are older ones.

   iii. **Unreliable visual fields or optic disc assessment.** The entire concept of following ocular hypertensive patients without treatment rests on the clinician’s ability to detect early damage. If this is not possible, treatment is indicated.

   iv. **A patient who is content** with treatment initiated by another physician and who is tolerating the medication well.

   v. **An ocular hypertensive patient who desires treatment.**

   vi. **An ocular hypertensive patient who has developed a vascular occlusion in either eye.**

3. **Additional factors** to consider include the

   i. Patient’s age,

   ii. Potential life span,

   iii. Adherence to therapy and follow-up visits,

   iv. And the ability to monitor disease progression with accurate assessments of the optic nerve (eg, anomalously optic nerves may be difficult to monitor) and reliable visual field tests.

   v. Quality of life issues such as cost and potential for side effects can and should play a significant role in the decision of whether or not to treat;

4. If a decision is made to **initiate treatment**, medication should be started as a therapeutic trial in one eye.

   i. Agents include adrenergic antagonists, brimonidine, latanoprost(alternate day PG) & topical CAI

   ii. Monotherapy is desirable with a maximum of two medications most of the time.

   iii. If common medical agents are not effective in lowering IOP / not well tolerated,

   ✓ argon or (low intensity selective laser trabeculoplasty can be considered

   ✓ or the patient can be followed closely without treatment;

   iv. Cataract surgery results in significant reduction of IOP

   v. More aggressive therapy should have a very strong rationale before employment. Thus, miotics, systemic carbonic anhydrase inhibitors, and filtering surgery are rarely used in ocular hypertensive patients.

**Conclusion** - Hence, early recognition and treatment of high risk patients can limit the visual disability due to POAG. Frequency doubling perimetry (FDP) or short wavelength automated perimetry (SWAP) detects glaucomatous damage at a very early stage, 4 years before the changes appear in white-on white perimetry. Hence, for patients under monitoring, FDP or SWAP may be beneficial in early initiation of treatment.
Ocular Hypertension Treatment Study (OHTS) Essentials

• **Purpose:**
  ✓ To evaluate the safety and efficacy of topical ocular hypotensive medications in preventing or delaying the onset of visual field loss and/or optic nerve damage in participants with ocular hypertension.

• **Participants:**
  ✓ 1637 patients with ocular hypertension recruited between 1994 and 1996.
  ✓ aged between 40-80 years and
  ✓ IOP values between 24-32 mm Hg in one eye
  ✓ without any evidence of glaucomatous damage were randomized to treatment and observation

• **Study design:**
  ✓ Multicenter randomized controlled clinical trial comparing observation and medical therapy for ocular hypertension.

• **Results 2002:**
  ✓ Topical ocular hypotensive medication was effective in delaying or preventing the onset of primary open angle glaucoma (POAG).
  ✓ The incidence of glaucoma was lower in the medication group than in the observation group (4.4% vs 9.5%, respectively) at 60 months’ follow-up.
  ✓ No increase in adverse events was detected in the medication group.
  ✓ The 5-year risk of developing POAG was associated with the following baseline factors: Using multivariate analysis
    1. **Older age**
       ✓ Age is an independent risk factor for the development of POAG.
       ✓ OHTS found an increased risk of POAG with age (per decade), of 43% in the univariate analysis and 22% in the multivariate analysis.
    2. **Higher pattern standard deviation**
       ✓ Although the patients with ocular hypertension may not have visual field defects on Standard Automated Perimetry (SAP),
       ✓ OHTS found that greater PSD on SAP correlated with increased risk of progression to POAG.
       ✓ 22% increase in relative risk per 0.2 dB increase
    3. **larger vertical and horizontal cup–disc ratios**
       ✓ Although OHT patients have no apparent glaucomatous disc changes, increased vertical and horizontal cup-disc ratio is a risk factor for progression to POAG.
       ✓ larger vertical and horizontal cup–disc ratios 32% and 27% increases in relative risk per 0.1 increase, respectively,
    4. **And higher baseline IOP**
       ✓ Studies have revealed the normal IOP range of 10-21 mmHg.
       ✓ Although, IOP readings may show considerable variations among glaucoma patients, IOP reading more than 22 mmHg is a positive predictive factor for the development of POAG.
       ✓ 10% increase in relative risk per 1 mm Hg increase.
    5. **Central corneal thickness (CCT)**
       ✓ was found to be most powerful predictor for the development of POAG
IOP assessed by applanation tonometry may be overestimated or underestimated in thicker and thinner corneas, respectively.

CCT less than 555µ were found to be at greater risk than eyes with CCT more than 588µ.

81% increase in relative risk for every 40 µm thinner.

6. **Family history and black race**
   - The corneas in OHTS participants were thicker than those in the general population, and African American participants had thinner corneas than others in the study.
   - The increased risk of glaucoma progression in black participants (on univariate but not multivariate analyses) may be attributed to their thinner corneas and greater cup-disc ratios.
   - A positive family history of glaucoma was not identified as a significant risk factor in this study, possibly because of inadequate assessment from self-reporting.

7. Other potential risk factors, such as myopia, diabetes mellitus, migraine, and high or low blood pressure, were not confirmed in the OHTS as significant risk factors for glaucomatous progression.

- **Results 2007:**
  - The OHTS prediction model for the development of POAG was independently validated in the European Glaucoma Prevention Study.

- **Results 2010:**
  - Topical ocular hypotensive medication was initiated in the original observation group after 7.5 years (median) without medication, and medication was continued for 5.5 years thereafter.
  - Participants in the original medication group continued topical ocular hypotensive medications for a median of 13 years.
  - The proportion of participants who developed POAG was 0.22 in the original observation group and 0.16 in the original medication group.
  - The primary purpose of the follow-up study was to determine whether delaying treatment resulted in a persistently increased risk of conversion to glaucoma, even after the initiation of therapy.
  - Although the two groups diverged with respect to the development of glaucoma during the original study period (when the observation group did not receive treatment), there was no further divergence in the Kaplan-Meier curves after both groups received IOP-lowering treatment.