Clinical Insights in Treating Glaucoma

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Clinical Insights

- Diagnosing and managing Ocular Hypertension and Glaucoma requires a series of decisions be made over the course of the lifetime of care
  - Is disease present?
  - What tests should be performed to aid in establishing diagnosis?
  - If disease is present, what type?
  - OHTN vs. Glaucoma
  - Is therapy required?
  - What therapy?
  - If glaucoma, what type?
  - Primary vs. secondary
  - Open vs. chronic angle closure
  - Grade severity of condition
  - Establish the target IOP
  - When should patient return?

When Do You Treat????

- Glaucoma
  - End-stage condition due to multiple etiologies
    - elevated IOP, toxicity, ischemia, connective tissue
  - Final common pathway with loss of ganglion cells
    - distinctive optic neuropathy
      - characteristic visual field loss not required
      - pre perimetric glaucoma
    - Optic nerve and/or visual field loss consistent with glaucoma regardless of IOP

The Glaucoma Continuum

Clinical Pearls Managing Glaucoma

- Pre Perimetric Glaucoma
  - Optic nerve changes consistent with glaucoma with full or borderline visual fields
  - IOP may be elevated
  - Early VF damage may be present on new tests
    - FDT Threshold, SWAP may reveal early damage
  - Nerve Imaging may also reveal early change
    - HRT II, GDX VCC, OCT 3
  - 2003 AAO Preferred Practice Guidelines
    - new definition of early glaucoma does not include visual field loss

- Ocular Hypertension
- Preperimetric Glaucoma
  - Optic Nerve Changes only
    - Is this Real?
  - Optic Nerve Changes and FDT Threshold and/or SWAP field loss
    - Is this Real?
When Do You Treat???

- **Glaucoma Suspect**
  - Ocular hypertension
    - IOP > 21 mm Hg w healthy optic nerves and visual fields
  - Asymmetric IOP
    - 5 mmHg or greater difference
  - Suspicious optic nerve
    - large cupping associated w large disc
  - Visual field loss
    - picked up on screening fields such as the FDT

When Do You Treat Ocular Hypertension?

Ocular Hypertension

- Until OHTS, therapy for OHTN was largely subjective
- Murray’s Rule one of first risk tools
- Now have evidence based approach to therapy

Risk of Progression From OHT to Glaucoma

![Risk Assessment](https://example.com)

Risk Assessment

- **Concept comes from Framingham Heart Study**
  - Begun in 1948 in Framingham, MA and continues to this day
  - Just after WWII, cardiovascular disease (CVD) was recognized as important contributor to morbidity and mortality in US
  - Little was known of causes for heart disease
  - Objective was to follow a group of individuals over a longer period of time to identify characteristics contributing to CVD

Benefit of Treating OHT

- 60% risk reduction in treated patients

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>10-year Risk of Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated patients</td>
<td>4.4%</td>
</tr>
<tr>
<td>Untreated patients</td>
<td>9.5%</td>
</tr>
</tbody>
</table>

Risk Assessment

- 5209 individuals enrolled b/w ages 30-62
  - None had symptoms of CVD or MI or CVA at time of study entry
  - All individuals underwent physical exam, interview and lab testing on a 2-year basis
  - 1971 Framingham II begun
    - Comprised of 5214 of original participants adult children and spouses
  - Currently Framingham III with goal to recruit 3500 grandchildren of original participants
  - Ongoing study has provided information on role of blood pressure, high cholesterol, smoking, obesity, diabetes and physical inactivity in development of CVD
Lessons From Cardiovascular Medicine
- Lifetime risk data need lifelong studies
- Early in the process, assumptions have to be made
- Risk models evolve with growing evidence
- Global risk is an essential part of management decisions

How Can This Strategy Be Applied to Glaucoma?
- Identify patients at moderate to high risk of converting from ocular hypertension to glaucoma
- Direct therapy at those who are at greatest risk
- Which risk factors should be considered?

Risk Assessment
- Consider number of risks individual has that puts them at risk for
  - conversion of ocular hypertension to the development of glaucomatous damage OR
  - from early glaucomatous damage to blindness
- Based upon evidence
- Studies include Ocular Hypertension Treatment Study
- What risk is too much and therapy is indicated prophylactically?
- Uses concept from Framingham Heart Study and Cardiovascular disease

Risk Assessment
- In cardiovascular disease, evaluate risk factors for conversion of hypertension to known outcome such as MI or CVA
  - Risks include hypertension, obesity, elevated cholesterol, smoking, family history, sedentary lifestyle
- Use similar risk factor assessment for the development of glaucoma
  - Outcome measure is not as obvious
  - When is glaucoma present?
  - Optic nerve damage only vs. nerve and field loss

Global Risk Assessment and Cardiology
- Risk assessment and prevention have contributed to the reduction in cardiovascular mortality

Risk Assessment
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Risk Assessment

• At what risk is therapy indicated to prevent undesirable outcome from occurring
• For glaucoma approximately 15% is consensus
• If cardiovascular disease, risk is approx 5%

Risk Assessment

• Ocular Hypertension to Glaucoma
  – Risk
• Glaucomatous Damage to Functionally Impaired (Blind)
  – 15 dB
  – Risk
  – Use 15 year time frame

Risk Assessment

OHTN to Glaucoma
Steve Mansberger, MD
www.discoveriesinsight.org
Discoveries in Sight Portland, OR

Risk Assessment

• Age
• IOP
• Corneal Thickness
• Vertical Cup/Disc Ratio
  – Optic Nerve healthy
• PSD Visual Field
  – Global Indice
  – Field full
• Diabetes Status
Risk Assessment

- Risk Level Low  < 5%
  - Monitor
- Risk Level Moderate  5-15%
  - Consider Therapy Discuss with patient
- Risk Level High  >15%
  - Treat

Table 1

Six Important Questions in Managing OHTN or POAG

- What is the risk to our patient’s visual function if condition is not treated?
- If we accept that OHTN and glaucoma has a natural history with a likely outcome that our patient and ourselves are not willing to risk, how early and aggressively must we treat to alter natural history and preserve vision?

Six Important Questions in Managing OHTN or POAG

- What are the downsides to treatment?
- Which treatment is best?
- How are the results of the treatment best measured?
- What risk factors help most in making the best management decisions?

OHTN Who Do You Treat?

- IOP > 30 mmHg
- Younger Individuals
- African Americans
- Family History
- Optic nerve
  - larger cupping or asymmetry
- Thin corneas < 530 um
- Borderline fields
OHTN Who Do You Treat?

• Age
  – Individuals living longer
  – 1 million people by 2050 over 100 years old
  – A new consideration
• Example
  – 79 yo WM w mild glaucoma
  – Brother 89 yo
  – Both parents lived into the 90s

Initial Medical Management of OAG

• Before starting therapy
  – obtain several IOP readings
    • either done on one day (diurnal curve) or over 2-3 days at different times
    • need detailed pretreatment information
      – medical and ocular
  – grade severity of glaucoma
    • based upon nerve appearance, fields and highest IOP

Describe and Understand Condition

• Open vs. Narrow Angle
  – Chronic angle closure glaucoma resembles open angle forms
    • detect with gonioscopy
    • Asians
• Primary vs. Secondary forms
  – detect with slit lamp evaluation
  – secondary glaucomas

Clinical Correlations in Glaucoma

• Compare the visual field and optic nerve appearance
• Does the disc and visual field correlate?
• Does the comparison between the right and left eyes fit?

Initial Medical Management of OAG

• Ask “How will optic nerve and visual field appear in twenty years”
  – not in 3 months
  – Hattenhauer
• Lower target IOPs
  – AGIS data
  – Sustained IOP reduction
• Target IOP is a range
  – “You Can’t Always Get What You Want”

Clinical Decisions in Glaucoma

• Target pressure
• Select therapy
  – Medications
    • Prostaglandins
    • Beta blockers
    • CAI
    • Adrenergic
  – Laser Trabeculoplasty
  – Filter Surgery
Selecting the Primary Medication
Open Angle Glaucoma

• Base the decision on:
  – Stage of disease
  – Baseline IOPs
  – General health of patient
  – Insurance coverage
  – Systemic medications
    • consider Brimonidine or Latanoprost if on systemic β-blocker

Select Target Pressure

• Think in terms of Per Cent Reduction from highest IOP reading
• Greater the damage, lower the IOP needs to be

Setting Target Pressures

• Consider the following:
  – How bad is the glaucoma?
  – How long did it take to get that bad?
    • get from old records if possible
  – What is the life expectancy of the patient?
• Trend is for lower target IOPs
  – sustained reduction

Target IOP Based Upon Initial Optic Nerve Damage and Highest IOP

<table>
<thead>
<tr>
<th></th>
<th>20 mm Hg</th>
<th>30 mm Hg</th>
<th>40 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>25%</td>
<td>30%</td>
<td>40%</td>
</tr>
<tr>
<td>Moderate</td>
<td>35%</td>
<td>40%</td>
<td>50%</td>
</tr>
<tr>
<td>Severe</td>
<td>45%</td>
<td>50%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Target IOP and Record Keeping

• In front of chart, record highest untreated IOP at time of diagnosis
• May also record target IOP in front of chart
• Also, as time goes on if find higher IOP, record this also
• Recognize that target IOP is tentative and as time goes by, this is the best guide to whether the target IOP is appropriate
• Remember one does not achieve everything
• If approach target, then need to judge whether additional risks are worthwhile to get there

AGIS- IOP Reduction and Field Change
AJO Oct. 2001
Target IOP

• If progression occurs, may need lower target IOP
• Target IOP is an educated guess
  – Some people may lead to more IOP lowering than needed and in others, not enough

Initial Medications

• PGs are the usual medication first used
  – Xalatan
  – Travatan
  – Lumigan
• Beta Blockers
• Alpha Agonists
• CAIs
• Fixed Combination - CoSopt

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Following Over Time

Modifying the Medical Regimen

Lack of Control

• IOP too high
  – Reverse Monocular Trial
• IOP Variability
• Optic Nerve Progression
• Visual Field Loss
• Adding a medication
  – medications vs. laser vs. filter surgery
  – add medication vs. increase dosage or concentration

Risk of Progression

Risk Factors for the Progression of Glaucoma

Risk Factors

Older age
Higher IOP (baseline)
Higher IOP (over follow-up)
IOP fluctuation
VF status at baseline
Race (nonwhite)
Disc hemorrhage
Pseudoexfoliation
**When do you Add or Switch a Medication**

- Switching is not usually a good strategy
  - Beware of “Regression to Mean”
- Tendency is to do nothing or add medications
  - Tolerance develops to some medications
    - Beta blockers, alpha agonists
- Is the angle getting narrow?
  - Perform gonioscopy

**Managing Glaucoma**

- First medication
  - Prostaglandin
- Second medication
  - Topical CAI or beta blocker
  - Or switch to different prostaglandin
- Third medication or modality
  - Fixed combination “Cosopt”
- Fourth medication or modality
  - Brimonidine or ALT/SLT
- Fifth modality- surgery

**Additivity to PGs**

- Topical CAIs
- Beta blockers
- Alpha agonists

**Topical CAI**

- Primarily used as adjunctive agent
  - May be used bid as adjunct agent w 20% additional reduction
- **May be best additive agent to prostaglandin**
- When used as monotherapy, requires tid dosage
- Rare systemic side effects
  - Metallic taste- 27%

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**Table 1: Intraocular Pressure Reduction of 5 Treatments to Various Agents Added to Latanoprost**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Number (n)</th>
<th>Mean Baseline IOP (mm Hg)</th>
<th>Mean IOP 1 Year (mm Hg)</th>
<th>Mean IOP Change 1 Year (mm Hg)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latanoprost</td>
<td>25</td>
<td>19.0</td>
<td>16.0</td>
<td>-3.0 (97%)</td>
<td>P &lt; .01</td>
</tr>
<tr>
<td>Dorzolamide</td>
<td>25</td>
<td>17.0</td>
<td>14.0</td>
<td>-3.0 (97%)</td>
<td>P &lt; .01</td>
</tr>
<tr>
<td>Timolol</td>
<td>10</td>
<td>24.0</td>
<td>16.0</td>
<td>-8.0 (98%)</td>
<td>P &lt; .01</td>
</tr>
<tr>
<td>Brimonidine</td>
<td>25</td>
<td>20.0</td>
<td>16.0</td>
<td>-4.0 (98%)</td>
<td>P &lt; .01</td>
</tr>
</tbody>
</table>

**Notes:**

1. IOP = intraocular pressure
2. Treated patients received latanoprost 0.005% ophthalmic solution twice daily
3. All patients were instructed to use the eye drop four times a day unless otherwise noted
4. Data were analyzed using the Mann-Whitney U test for non-parametric data
Adjunctive Therapy

• Most patients require more than 1 medication over their lifetime
• Medication added when
  – IOP too high
    • above target pressure
  – Visual Field Progression
  – Optic Nerve Progression

When is surgery indicated?

• Poor control
  – progression noted in optic nerve or v. fields
  – account for variability on visual fields
    • repeat test to confirm change
• IOP above target pressure
  – exhausted several or all medical options
• Medication side effects
• Poor compliance

Communication in the Management of Glaucoma

• Patient’s decision to use glaucoma medication is result of balance between
  – Their understanding potential risks of glaucoma
  – Their belief in the benefit of medication
  – Burden in taking their drops
• For most patients risk of untreated glaucoma concerns potential loss of vision
• On the other hand burden of treatment is not an abstract idea but a tangible daily experience

Communication in the Management of Glaucoma

• Although glaucoma therapy is not as burdensome as some other conditions, it is still vulnerable to all the barriers of adherence as with any chronic condition as well as having some unique problems
• Inconvenience, cost, and integration into daily life are reasons for poor adherence
• Clinician-patient communication is the foundation of adherence and adherence is the key factor in treatment

Communication in the Management of Glaucoma

• Clinicians Can Not Detect Nonadherence
  – Research has shown clinicians have no better than a 50:50 chance of detecting nonadherence
  – Patients w treatment resistant hypertension who told their doctors that they were taking their medication consistently
    • Told to continue with their current tx regimen using a pillbox that would record when they took meds
    • Subjected to this scrutiny, 1/3rd instantly cured
      – Several had syncopal episodes when they complied b/c regimens had been intensified in mistaken belief that they had been adherent
      – Another 20% remained uncontrolled but recording pillbox demonstrated nonadherence

Communication in the Management of Glaucoma

• Barriers to detecting nonadherence: the psychology of patient self reporting
  – Patients do realize that providing misinformation may lead to poor decisions about tx but their behavior is shaped by a more powerful force
    • Nonadherence is a socially undesirable behavior and patients want to be seen as “good patients”
    • Also, patients expect their doctors to be “Judgmental”
  • Need to reverse judgmental environment and redefine the “good patient” as one who collaborates in solving treatment problems
Communication in the Management of Glaucoma

- **Detecting and Intervening- Four Step Approach**
  - Begin with open-ended question “Tell me how you’ve been taking your medications”
  - Response will reveal understanding of tx regimen
  - Follow up with question about how they remember to take medication(s)
  - It is useful to have patient describe the way they use all their medications
    - both topical and systemic

- **Change the patient’s expectation that you will be judgmental**
  - Tell patient that you know that everyone may miss a drop occasionally
  - Explain how information about adherence will affect decisions about medication
  - Change dynamic so that a “good” patient is one who discusses and solves problems with adherence with the clinician

- **Finally, ask about forgetting or missing medications**
  - This fourth step comes last, after the stage has been set
  - When problems with adherence are discovered, evaluate patient’s motivation to adhere and presence of specific barriers
    - Strategy is to determine that pt is concerned about consequences of glaucoma and believes tx will be beneficial

- **From the Ask – Tell – Ask Sequence, understand what patient knows, doesn’t know, and the patient’s misconceptions and mistaken beliefs**
  - In this example, clinician learns that patient
    - Knows their pressure is too high
    - Doesn’t understand why medication was started now and not before
    - Has mistaken belief that they do not have glacoma unless experiencing vision loss

- **Telling the patient what they already know is not time efficient**
  - Many clinicians use the same glaucoma speech
    - In this example, clinician can tell patient their “IOP is too high, that does produce glaucoma if not corrected and it is time for medication in your case”
Communication in the Management of Glaucoma

- Tell patient key missing information
  – In this example, clinician can tell patient that “high IOP is not the whole story of glaucoma and when you need treatment. The pressure causes damage to the nerve that goes from the eye to the brain, and we detected the beginning of damage at the last visual field. That is why we know that you need treatment”

- Tell the patient about their misconceptions and mistakes
  – Perhaps the most important benefit of asking before telling is the opportunity to identify the patient’s misconceptions
  – Erroneous beliefs dramatically interfere with patient’s motivation to adhere and self-care behaviors
  – Striking how prevalent and unpredictable mistaken beliefs can be across all chronic diseases.
  – The only way to discover mistaken beliefs is to ask

- In this example, the patient’s response is
  “A lot of people believe that they do not have glaucoma unless they notice a problem with their vision. We can detect the problem of glaucoma before you can yourself, and that is a good thing because it gives us a chance to prevent more serious damage”

- The second ask reveals what has happened to the patient’s understanding as a result of the “tell”
  – “What questions or concerns do you have now that you have heard what I just told you?”
  – Takes the dialog to the next step of explanation

- In this example the patient’s response is
  “So you mean I’ve already got damage to my eye? How bad is it? You said the medicine will prevent more serious damage?”

- The second ask continues the dialog and lets the clinician know which parts of the “tell” got through
- Our patient’s response to the second ask makes it clear that the patient needs to learn a little more about the stage and severity of her problem and is ready to hear a reassuring link between the medication and preventing vision loss

<table>
<thead>
<tr>
<th>Learned from the first “ASK”</th>
<th>Focus of the “TELL”</th>
<th>Learned from the second ASK</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. What the patient already knows that is correct and important.</td>
<td>Reinforce without wasting time.</td>
<td>Assess improvement in confidence, self-efficacy, and commitment.</td>
</tr>
<tr>
<td>2. What the patient doesn’t know that they should.</td>
<td>Prioritize and present the next most important pieces of information.</td>
<td>Assess comprehension and impact of new information.</td>
</tr>
<tr>
<td>3. The patient’s misconceptions and mistaken beliefs.</td>
<td>Correct misconceptions and mistakes.</td>
<td>Assess comprehension and impact of corrected understanding and beliefs.</td>
</tr>
</tbody>
</table>