Clinical Insights into the Treatment of Glaucoma

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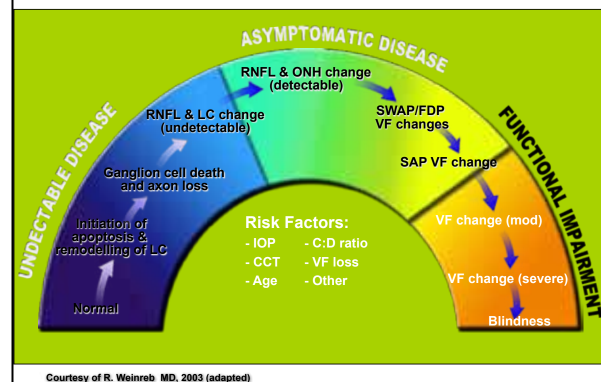
Clinical Insights

- 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



Courtesy of R. Weinreb MD, 2003 (adapted)

When Do You Treat????

- Pre Perimetric or Early 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

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?

- 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

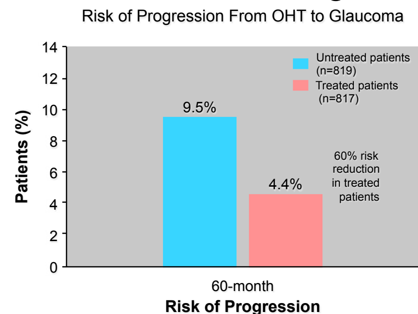
- What are the downsides to treatment?
- Which treatment is best?
- How are the results of the treatment best measured?
- What risk factors help most in making the best management decisions?

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

The Ocular Hypertension Treatment Study
A Randomized Trial Determines That Topical Ocular Hypotensive Medication Delays or Prevents the Onset of Primary Open-Angle Glaucoma

Benefit of Treating OHT



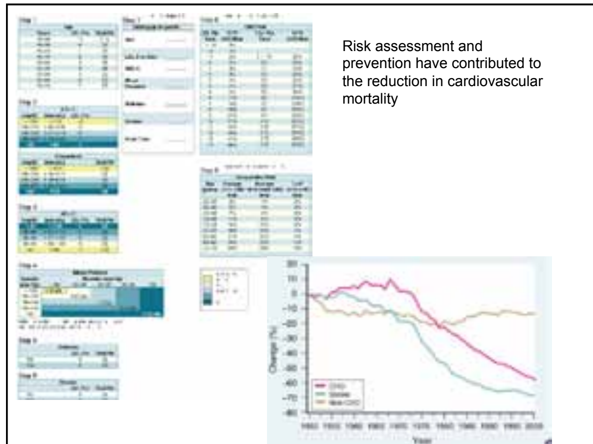
OHT = ocular hypertension.
Kass MA et al. *Arch Ophthalmol.* 2002;120:701-713.

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

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



Risk assessment and prevention have contributed to the reduction in cardiovascular mortality

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

Risk Assessment

- Ocular Hypertension to Glaucoma
  - Assess risk
- Glaucomatous Damage to Functionally Impaired (Blind)
  - 15 dB
  - Risk
  - Use 15 year time frame

Risk Assessment

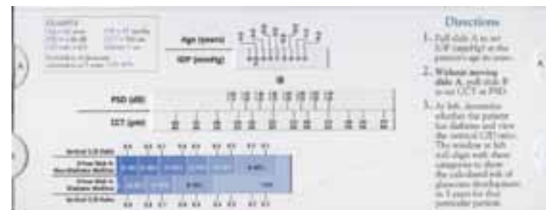
- Age
- IOP
- Corneal Thickness
- Vertical Cup/Disc Ratio
  - Optic Nerve healthy
- PSD Visual Field
  - Global Indice
  - Field full
- Diabetes Status

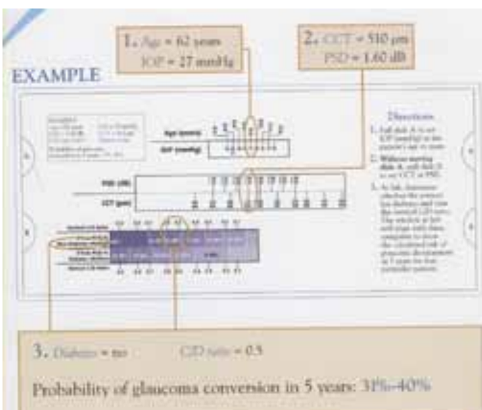
Risk Assessment
OHTN to Glaucoma
www.discoveriesinsight.org
Discoveries in Sight Portland, OR

Risk Assessment

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

STAR Calculator I





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
    - driver for choosing initial therapy
  - Baseline IOPs
  - General health of patient
  - Insurance coverage and patient's ability to afford medications
  - Systemic medications being used
    - 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 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

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 (latanoprost) - generic
  - Travatan Z (travoprost)
  - Lumigan (bimatoprost) – 0.01, 0.03
- Beta Blockers – Useful first line option, especially with cost as a consideration
  - Timolol, Levobunolol, Betaxolol
- Alpha Agonists
  - Brimonidine 0.1, .15, .2
- CAIs – Excellent 2nd line agent
  - Trusopt (dorzolamide), Azopt (brinzolamide)
- Fixed Combination Agents
  - CoSopt (Timolol-Dorzolamide), Combigan (Timolol-Brimonidine)

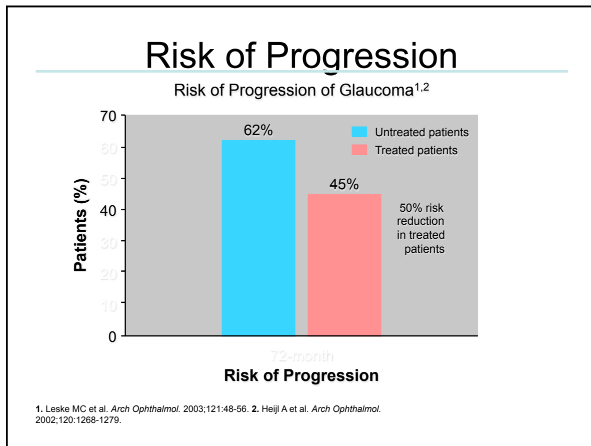
Generic Medications

- Currently available ophthalmic glaucoma drugs in generic form
  - Beta blockers
    - Timolol, levobunolol, carteolol
  - Alpha-adrenergic agonist
    - Brimonidine 0.15, 0.2%
  - Topical carbonic anhydrase inhibitor
    - Dorzolamide
  - Parasympathomimetics
    - Pilocarpine
  - Fixed Combination
    - Dorzolamide/timolol
  - Oral carbonic anhydrase inhibitors
    - Acetazolamide
    - Methazolamide

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



1. Leske MC et al. *Arch Ophthalmol.* 2003;121:48-56. 2. Heijl A et al. *Arch Ophthalmol.* 2002;120:1268-1279.

Risk Factors for the Progression of Glaucoma

Risk Factors
Older age[1-3]
Higher IOP (baseline)[2]
Higher IOP (over follow-up)[2]
IOP fluctuation[4]
VF status at baseline[2]
Race (nonwhite)[3,5]
Disc hemorrhage[2,5]
Pseudoexfoliation[2]

When do you Add or Switch a Medication

- Switching is not usually a good strategy
  - Beware of "Regression to Mean"
  - Going from one PG to another may help
- 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 or Beta Blocker
- 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

Table 1. Intraocular Pressure Reduction at 1 Year by Various Agents Added to Latanoprost

Medication	Number of Eyes	Mean Baseline IOP (mm Hg)	Mean IOP at 1 Year (mm Hg)	Mean IOP Change (mm Hg [%])	P Value*
Dorzolamide ALL	26	19.8	16.0	−3.9 (19.7%)	P < .001
Dorzolamide BID	11	20.5	16.6	−3.9 (15.4%)	P < .001
Dorzolamide TID	14	19.4	15.5	−3.8 (19.9%)	P < .001
β-blockers	22	19.9	17.4	−2.5 (12.2%)	P < .001
Brimonidine	26	21.0	19.0	−2.0 (9.3%)	P = .0019

BID = twice a day; IOP = intraocular pressure; TID = three times a day.

[*] P values are for change from latanoprost baseline.

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%

Adjunctive Therapy

- Most patients require more than one 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

Surgical Options

- Laser Trabeculoplasty
  - ALT, SLT
- Filter surgery – trabeculectomy
  - With MMC/5-FU
  - Gold standard but associated with short and long term complications
    - Often complication related to bleb
- Valves
  - Molteno, Baerveldt
- New procedures
  - Express implant, Trabecutome, Canaloplasty

Surgical Management of Glaucoma

- At the beginning of the revolution in surgical care of glaucoma
- Minimally invasive glaucoma surgery is now a possibility
- Examples
  - Ab interno trabeculectomy using a device
    - Trabectome, Neomedix
  - Canaloplasty using a microcatheter
    - iTrack, iScience Interventional
    - Circumferential viscodilation of Schlemm's canal with placement of a trabecular tensioning-suture
- IOP reduction is not as low as with trabeculectomy but the risks are considerably less and appropriate for select patients

Surgical Management of Glaucoma

- Other surgical approaches under review
  - Trabecular micro-bypass device
    - iStent, Glaukos
    - Facilitates aqueous flow into Schlemm's canal by bypassing the major site of resistance in the TM
  - GMS Plus Gold Shunt
    - SOLX
  - Cy-Pass
    - Transcend Medical
  - Last two devices shunt aqueous humor from anterior chamber directly into the suprachoroidal space
- Due to the safety of these new procedures, surgeons are more apt to consider combined cataract-filtration surgery b/c of the reduced risk of the glaucoma procedure

Surgical Management of Glaucoma

- Three surgical approaches
  - The Express mini-implant
    - Used with conventional trabeculectomy
    - Device placed under the flap
    - Standardize procedure including size of opening
    - Prevents eye pressure from getting too low in immediate post-operative period
  - Trabectome
    - Removes tissue from inside the eye (trabecular meshwork) using electro-surgical hand piece to disrupt tissue
  - – Canaloplasty
    - Dilation of the entrance to the outflow pathways found in the wall of the eye (Schlemm's canal)

Surgical Procedures

- In recent years, technologies have become available that seek to avoid the complications of traditional filtration surgery by accessing the eye's natural aqueous drainage pathways and enhancing them
- Most of these technologies seek to avoid a filtration bleb that can be the source of infection, discomfort, and other problems
- These technologies represent a shift in focus and skills, yet seek to accomplish the goal of lowering intraocular pressure sufficiently to prevent vision loss from glaucoma

Patient Communication Ask-Tell-Ask

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