Evidence-Based Approach to Managing Glaucoma

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Background

David Eddy, M.D., Ph.D.
- Heart surgeon turned health-care economist
- Coined term “evidence-based medicine”
- Early 1980’s questioned outcomes of glaucoma treatment
  - Suggested treatment was harmful
- Stimulated clinical trials
Introduction

- Evidence-based medicine
  - How that applies to glaucoma care
- Summary of major clinical glaucoma trials
  - 6 landmark studies
- Imaging technology
  - Early detection
  - Measurement of progression
Studies

1. Ocular Hypertension Treatment Study (OHTS)
2. European Glaucoma Prevention Study (EGPS)
3. Early Manifest Glaucoma Study (EMGS)
4. Collaborative Initial Glaucoma Treatment Study (CIGTS)
5. Advanced Glaucoma Intervention Study (AGIS)
6. Collaborative Normal-Tension Glaucoma Study (CNTGS)
1. Ocular Hypertension Treatment Study (OHTS)

- What is the risk of developing glaucoma in patients with elevated pressure alone? (normal nerve and VF)
- 1600 patients
  - 800 medical treatment
    - Goal of reducing IOP by 20%
    - 4.4% progressed to glaucoma
  - 800 observation only
    - Twice yearly for 5 years
    - 9.5% progressed to glaucoma
- 50% lower risk for developing glaucoma in the treated group compared to untreated
- 90% of untreated patients did not develop glaucoma over 5 years
- Glaucoma can develop in patients with OHT
- Lowering IOP can prevent OHT from converting to glaucoma
OHTS Risk Factors

- Thinner Central Corneal Thickness (CCT)
  - Most prominent factor for predicting which patients progress to glaucoma over 5 years
- Older Age
- Higher IOP
- Larger Cup/Disc Ratio
- Create a risk profile for which patients may develop glaucoma and tailor treatment
  - [http://ohts.wustl.edu/risk/calculator](http://ohts.wustl.edu/risk/calculator)
2. European Glaucoma Prevention Study (EGPS)

- What is the likelihood of preventing glaucoma using topical dorzolamide alone?
- Patient population similar to OHTS
  - Followed 5 years
  - Half treated with dorzolamide
    - IOP lowered by 22%
  - Half treated with placebo
    - IOP lowered by 20%
  - Dorzolamide does not help in prevention of glaucoma
- Validated same risk factors as in OHTS (CCT, IOP, age, elevated cup/disc ratio)
3. Early Manifest Glaucoma Trial (EMGT)

- 255 subjects newly diagnosed with disc damage, field loss
- Disease progression based on repeatable VF loss or optic disc
  - **Treatment group with betaxolol + 360° ALT**
    - Avg. IOP reduction by 25%
    - 45% progressed but delayed
    - Treatment benefit not large
  - **Observation group**
    - 62% progressed
  - Q 3 months visit for 6 years
- Same risk factors as OHTS
- This study allows us to follow natural history of glaucoma
- If we leave people alone who have glaucoma, they will get worse over time
- **Every 1 mmHg lower IOP reduces risk of progression by 10%**
4. Collaborative Initial Glaucoma Treatment Study (CIGTS)

- What is the best way to treat glaucoma patients with disc damage and VF defect: surgery or medication as initial treatment?
- 600 patients
  - Trabeculectomy
  - Medication
- Success defined by VF score and achievement IOP goal
- With medication: IOP reduced by 38%
- With surgery: IOP reduced by 45%
- Both groups had stable VF at 5 years; data does not support notion of performing surgery first
5. Advanced Glaucoma Intervention Study (AGIS)

- What is the role of ALT in patients with advanced glaucoma?
- 700 eyes
  - ALT as initial treatment
  - Trabeculectomy as initial treatment
- Followed up to 11 years
- No overall difference in outcome between groups
- Reduction in IOP prevented VF loss
- Fluctuation in IOP had important effect on VF
- IOP <18mmHg at every visit had no change in VF over 8 years
6. Collaborative Normal Tension Glaucoma Study (CNTGS)

- Patients with glaucoma, VF loss, and disc damage, despite IOP < 20mmHg
- 140 patients followed q 3 months for 5 – 7 years
  - Conventional treatment
    - Goal of 30% reduction in IOP
    - 12% glaucoma worsened
  - Observation
    - 35% glaucoma worsened
- **Risk factors for progression:** female gender, migraines, vasospastic disorders, disc hemorrhage
Pearls from Clinical Trials

- Reduction of IOP lowers risk for glaucoma
- Treat “at risk” OHT patients with goal of reducing IOP by 20% to cut risk of glaucoma in half
- CCT strongly correlates with developing glaucoma if OHT present
- Treat patients with established glaucoma with goal of reducing IOP by 30%
- Glaucoma possible in patients with “normal” IOP
  - 33% never have “abnormal”
- Surgery as effective as medication; consider side effects
Diagnostic Methods

- Glaucoma still requires clinical diagnosis
- No single definitive test available
- New imaging technology may facilitate earlier diagnosis (GDx, HRT, OCT)
  - Detection of glaucomatous degeneration of Retinal Nerve Fiber Layer (RNFL) is valuable in early diagnosis because it may precede cupping and VF loss
Glaucoma Definition

- Optic neuropathy characterized by progressive injury to retinal ganglion cells and their axons (RNFL)
- Specific pattern of optic atrophy “cupping”
- Associated VF deficit
Retinal Nerve Fiber Layer (RNFL)

- Composed of axonal fibers of retinal ganglion cells
- Thickest superotemporally and inferotemporally
- Thinnest nasally and temporally
Intraocular Pressure

- Inaccurate as diagnostic indicator of glaucoma
- 90% with IOP ≥ 21mmHg do not have glaucoma
- 50% with glaucoma have IOP < 21mmHg
- Poor criterion for progression
Visual Field

- Gold standard for monitoring vision loss
- Limitations
  - May lose up to 40% optic nerve fibers before VF loss detected
- OHTS required triple confirmation of VF defects
  - 86% patients with “abnormal” VF result had normal VF when retested
  - Requires attentive, responsive patient
Optic Nerve Imaging Technology

- Identifies location of disease
- Damage to RNFL often precede VF loss
- Provides objective evaluation of structural damage in glaucoma
- Predictive tool for VF loss and disc deterioration
- Follow progression
Heidelberg Retinal Tomography (HRT)

- Confocal scanning laser ophthalmoscopy
- Provides topographic optic nerve head analysis
HRT

- Rim area measurements
  - Most promising for monitoring changes over time
GDX Nerve Fiber Layer Analyzer

- Scanning laser polarimetry
- Evaluates RNFL thickness
  - Rates of change provides parameter to evaluate which eyes are at risk for progression
NFI – Nerve Fiber Indicator
- Value from 0 - 100
- Most effective indicator for early diagnosis of glaucoma
Circular scan taken around optic nerve to measure RNFL thickness
RNFL thickness on OCT had highest sensitivity for detecting early changes in glaucoma suspect eyes
Cirrus HD-OCT outperforms Stratus OCT
- In detecting more eyes with RNFL defects
- Can detect changes in RNFL sooner
OCT

- RNFL thickness deviation map allows visualization of RNFL defects
- Provides sensitive strategy to analyze progression
THANK YOU