CONTROVERSIES IN GLAUCOMA

2013
AFOS Meeting
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QUESTION

IS ONE IOP READING ENOUGH?
INTRAOCULAR PRESSURE

- BALTIMORE EYE SURVEY (1991)
  - 5308 PATIENTS
  - BLACK AND WHITE
  - > 40 YEARS OLD
  - COMPREHENSIVE EYE EXAMS
  - GLAUCOMA DIAGNOSIS BASED ON ONH EVAL AND VF
  - OF THOSE FOUND TO HAVE GLAUCOMA
    - 55% HAD INITIAL IOP < 22
    - 24% < 22 ON TWO READINGS
    - 16% < 22 ON THREE READINGS
DIURNAL IOP

IOP PEARLS

- **NOT PART OF THE DEFINITION OF GLAUCOMA**
  - A RISK FACTOR ONLY
- **IF NOT ELEVATED, NO GUARANTEE OF NORMALCY**
- **IF ELEVATED, RULE OUT SECONDARY CAUSES**
- **REGARDLESS, IF SUSPICIOUS…**
  - GATHER OLD DATA
  - IF ALREADY TREATED AND UNSURE OF HIGHEST IOP
    - CONSIDER DRUG HOLIDAY / WASHOUT TO RE-ESTABLISH IOP BASELINE
  - TAKE MULTIPLE PRE-TREATMENT IOP READINGS
    - 2 MORNING, 1 AFTERNOON
- **ESTABLISH THE BASELINE IOP**
  - FOR TARGET
  - FOR MEDICATION EFFECTIVENESS
QUESTION

IS PACHYMETRY AN IOP FIX OR IS THERE MORE TO IT?
OCULAR HYPERTENSION TREATMENT STUDY (OHTS)

- 1300 PATIENTS

RESULTS
- IOP TREATMENT
  - LOWERING IOP DELAYS OR PREVENTS DEVELOPMENT OF GLAUCOMA IN PATIENTS WITH ELEVATED IOP
  - MAJORITY OF OCULAR HTN PATIENTS DO NOT DEVELOP GLAUCOMA
  - ALL PATIENTS WITH OCULAR HTN DO NOT NEED TX
  - TX THOSE AT GREATEST RISK
- CCT
  - INFLUENCES GOLDMANN TONOMETRY
  - THICKNESS < 555 um HAVE 3X RISK COMPARED TO > 588

IOP AND PACHYMETRY ADJUSTMENTS

“THE IMPLICATION THAT IOP CAN BE CORRECTED WITH AN ARITHMETIC, LINEAR CORRECTION FACTOR OF SOME mmHg / um CLEARLY REPRESENTS AN OVERSIMPLIFICATION OF WHAT IS UNDOUBTEDLY A COMPLEX AND NONLINEAR RELATIONSHIP BETWEEN CORNEAL THICKNESS AND TRUE IOP”

BRANDT JD, ET AL
OHTS, OPHTHALMOLOGY 2001; 108: 1779-1788
PACHYMETRY

- RACIAL VARIATIONS ARE PRESENT
  - AFRICAN AMERICAN 534 um
  - LATINO 546 um
  - CAUCASIAN 556 um
- NOMOGRAMS DO NOT AGREE
- SOLUTION
  - THINK: THIN / NORMAL / THICK
CCT PEARLS

- Pachymetry should be part of work-up for:
  - Ocular hypertension, glaucoma suspects, glaucoma
- A thin cornea is a risk factor for converting from ocular hypertension to glaucoma (OHTS)
- Errors can occur if off axis
  - Consider repeating anomalous readings or in few years
    - Look for consistent results, more likely believe thin than thick
- Don’t adjust the IOP, think: thin / normal / thick
- Consider
  - Pascal dynamic contour tonometry
    - IOP reading supposedly independent of CCT
  - Ocular response analyzer
    - Measures IOPG, IOPCC, corneal hysteresis and resistance factor
    - Low hysteresis associated with glaucoma
QUESTION

TRUE OR FALSE, YOU CAN TELL A PATIENT HAS GLAUCOMA BY THE C/D?
WHICH ONE OF THESE PATIENTS DO YOU THINK HAS GLAUCOMA?
C/D RATIO

“WHEN A CLINICIAN EXAMINES A PATIENT FOR THE FIRST TIME, THERE IS NO WAY TO DETERMINE WHETHER THE C/D RATIO OBSERVED HAS BEEN STABLE DURING THE PATIENT’S LIFETIME OR HAS ENLARGED AS PART OF THE DISEASE PROCESS, ASSUMING THAT NO PREVIOUS PHOTOGRAPHS OR MEASUREMENTS ARE AVAILABLE FOR COMPARISON”

GORDON MO, ET AL.
THE OHTS: BASELINE FACTORS THAT PREDICT THE ONSET OF POAG
ARCH OPHTHALMOL 2002; 120: 701-713.
CUP / DISC RATIO

- NO LINE SEPARATES NORMAL FROM GLAUCOMA
- NORMAL VERTICAL C/D RATIO VARIES FROM 0.00-0.85
- C/D RATIO OF $\geq 0.65$ OCCURS IN 2.2 - 4% OF NORMALS
- C/D RATIO IS A FUNCTION OF DISC DIAMETER
HOW TO MEASURE OPTIC DISC DIAMETER

• USE 60D LENS AT SLIT LAMP
  • IF NOT, USE CORRECTION FACTOR
• MAKE THIN VERTICAL BEAM
• ADJUST BEAM HEIGHT
• READ HEIGHT OFF SCALE
  • > 2.2 mm IS A LARGE DISC
  • < 1.8 mm IS A SMALL DISC
  • THIS IS A ROUGH ESTIMATE
    • REFRACTIVE ERROR / WORKING DISTANCE INFLUENCE READINGS
• OTHER METHODS
  • CAMERAS WITH SOFTWARE
  • ADVANCED IMAGING DEVICES
    • HRT
      • CALCULATES DISC AREA AND INDICATE SMALL / AVG / LARGE
    • OCT
      • CALCULATES DISC AREA

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Expected Physiologic Cup Size Based on Measured Vertical Disc Diameter Using a 60 Diopter Lens At The Slit Lamp

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Expected C/D ratio

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WHAT ELSE TO LOOK FOR

- GLAUCOMATOUS ONH SIGNS
  - VERTICAL ELONGATION
  - DIFFUSE RIM LOSS
  - RIM NOTCH
  - PERIPAPILLARY ATROPHY
  - DISC HEMORRHAGES
  - C/D ASYMMETRY > 0.2
  - ACQUIRED ONH PIT
  - NERVE FIBER LAYER DEFECTS
  - PROGRESSIVE CHANGE
THE ISNT RULE

• FIRST REPORTED BY JONAS ET. AL 1988
  • 457 NORMAL EYES
    • INFERIOR RIM > SUPERIOR > NASAL > TEMPORAL
  • GLAUCOMA VIOLATES THE RULE

• HOWEVER, NOT ALWAYS
  • 2006 STUDY ARCH OPHTHALMOL
    • 66 NORMAL EYES, 43 WITH OAG
    • ISNT RULE INTACT IN 79% OF NORMALS VS 28% OF OAG (P<0.001)
GLAUCOMATOUS ONH PEARLS

- A BIG CUP DOES NOT NECESSARILY MEAN GLAUCOMA
  - LARGE DISCS EXPECTED TO HAVE LARGE CUPS
  - SMALL DISCS EXPECTED TO HAVE SMALL CUPS
  - A SMALL DISC WITH A MEDIUM SIZE CUP CAN BE AS SUSPICIOUS AS A LARGE CUP IN A MEDIUM SIZE DISC
- GLAUCOMA CAN STILL OCCUR IN A BIG DISC. BE CAREFUL!
- NORMAL NERVES USUALLY FOLLOW THE ISNT RULE
  - BUT IT ISNT 100% FULLPROOF
- GLAUCOMA IS A PROGRESSIVE OPTIC NEUROPATHY
  - DILATE YOUR PATIENTS, LOOK STEREOSCOPICALLY AT ONH
  - DOCUMENT RIM HEALTH (THINNING), PPA, HEME, NFL, ETC.
  - RECORD MORE THAN JUST THE C/D
  - TAKE PHOTOS, MONITOR FOR CHANGE
HOW DO I KNOW IF A VISUAL FIELD IS GLAUCOMATOUS?
VISUAL FIELDS

• FIELD LOSS IS AN INDICATOR OF ADVANCED DISEASE
• EARLY IN DISEASE
  • FOLLOW OPTIC NERVE FOR CHANGES
• LATE IN DISEASE
  • FOLLOW VISUAL FIELD FOR CHANGES
    • MAY HAVE TO CONSIDER 10-2, MACULA
    • ESTERMAN FOR DRIVING, KINETIC III4E FOR LEGALLY BLIND
• COMMON GLAUCOMATOUS VF DEFECTS
  • THE ARCUATE DEFECT
  • THE NASAL STEP
  • THE PARACENTRAL DEFECT
  • DIFFUSE VISUAL FIELD LOSS
MINIMUM DIAGNOSTIC CRITERIA

KATZ, SOMMER, GAASTERLAND, ANDERSON (ARCH OPHTHAL 1991)

- TWO “OUTSIDE NORMAL LIMITS” ON GHT
  OR
- CLUSTER OF THREE OR MORE POINTS IN A LOCATION CHARACTERISTIC FOR GLAUCOMA, ALL DEPRESSED ON PATTERN DEVIATION PLOT AT A P < 5% AND ONE DEPRESSED AT A P < 1% ON TWO CONSECUTIVE FIELDS (24-2 COUNTS EDGE POINTS, 30-2 ONLY COUNTS 2 NASAL PTS), ALL PTS RESPECT HORIZONTAL MERIDIAN

OHTS (30-2 STRATEGY, ARCH OPHTHALMOL 1999)

- RELIABLE = LESS THAN 33% FP, FN, FL
- NORMAL = MD, PSD, SF, CPSD WITHIN 95% OF NORMALS, GHT WNL
- ABNORMAL = CPSD OUTSIDE 95% NORMALS OR GHT ONL
- VF REVIEWED, DETERMINE IF GLAUCOMATOUS, REPEATABLE X 3
VISUAL FIELD PEARLS

- DON’T ALWAYS BELIEVE THE VISUAL FIELD
- THE VISUAL FIELD MUST MATCH THE OPTIC NERVE
- LEARNING CURVES
  - CONSIDER TESTING THE POORLY TESTING EYE FIRST
  - CONSIDER CHANGING FROM SITA-STD TO SITA-FAST AS NEEDED
- USE ESTABLISHED CRITERIA TO DETERMINE IF VF IS GLAUCOMATOUS
  - REMEMBER HOWEVER NO SINGLE CRITERION IS PERFECT
- REPEAT THE VISUAL FIELD (1-2x) TO CONFIRM A DEFECT
- A NUMBER OF PATIENTS ARE POOR VF TAKERS
  - FOLLOW OBJECTIVE DATA (IOP / ONH) AND NOT VF
QUESTION

CAN YOU HAVE A NORMAL VISUAL FIELD AND STILL HAVE GLAUCOMA?
BACK TO THE QUESTION…

• CAN YOU HAVE A NORMAL VISUAL FIELD AND STILL HAVE GLAUCOMA?
  • YES
    • THIS IS CALLED PREPERIMETRIC GLAUCOMA
    • TYPICALLY STRUCTURAL LOSS PRECEDES FUNCTIONAL LOSS BUT THIS IS NOT 100%
      • BE CAREFUL
THE GLAUCOMA CONTINUUM

Weinreb RN et al. AJO. September 2004
THE NERVE FIBER LAYER

- 1-1.5 MILLION GANGLION CELLS
- AXONS CROSS RETINA
- CONVERGE ON THE ONH
- SUPERFICIAL BENEATH ILM
- TRAVEL IN ORGANIZED PATTERN
- REFLECT LIGHT BACK
- THE THICKER THE NFL THE BRIGHTER THE STRIATIONS
- BEST SEEN AGAINST A DARK BACKGROUND
NORMAL NFL FEATURES

- FINE WHITE LINEAR STRIATIONS
- IN ANTERIOR RETINAL LAYER
- BRIGHT STRIATIONS WITH A FULMINANT, COARSE TEXTURE
- CAST A WHITE HAZE OVER THE UNDERLYING RETINAL LAYERS
- TERTIARY BLOOD VESSELS ARE HIDDEN BENEATH THE NFL
- BECOMES BRIGHTER AS YOU GET CLOSER TO THE ONH
- MOST PROMINENT IN THE SUPERIOR AND INFERIOR ARCADES
- BRIGHT-DIM-BRIGHT PATTERN
NFL EVALUATION TECHNIQUE

- DILATED PUPIL
- CLEAR 78D LENS AT SLIT-LAMP
- MAXIMUM ILLUMINATION
- USE THE RED-FREE (GREEN) FILTER
- EXAMINE SUPERIOR AND INFERIOR
- COMPARE DIFFERENCES BETWEEN THE EYES
- ALSO
  - TAKE RED FREE PHOTOS
  - REVIEW THEM CAREFULLY
  - REPEAT AT REGULAR INTERVALS LOOKING FOR NFL CHANGE
THE NFL AND GLAUCOMA

- NFL THICKNESS
  - NORMALS > OC HTN > GLAUCOMA
- NFL LOSS AND VISUAL FIELDS
  - 60% HAVE VISIBLE NFL LOSS 4-6 YRS BEFORE VF LOSS
  - 88% EYES THAT DEVELOP VF LOSS HAVE NFL DEFECTS
  - NFL DEFECT CORRELATES WITH LOCATION OF VF LOSS
  - DEFECTS MORE FREQUENT WITH ESTABLISHED VF LOSS
NFL SLIT DEFECT

- EVIDENCE OF FOCAL OPTIC NERVE DAMAGE
- LARGER THAN AN ARTERIOLE WIDTH IN SIZE
- TRAVELS ALL THE WAY BACK TO THE NERVE
- ¼ mm WIDE = 50 um LOSS
- 50 um LOSS = 15,000 FIBERS
- 15,000 FIBERS = 1% OF TOTAL
NFL WEDGE DEFECT

- EASIEST TO IDENTIFY BUT THE LEAST COMMON
- REPRESENTS EXPANDING LOSS OF GANGLION CELLS
- ASSOCIATED WITH NOTCHING OF OPTIC NERVE
- ASSOCIATED WITH A VISUAL FIELD DEFECT
- MAY OCCUR AFTER DISC HEME
NFL DIFFUSE LOSS

- MOST COMMON NFL LOSS
- HARDEST TO IDENTIFY
- LOSS OF STRIATIONS IN THE SUPERIOR AND INFERIOR ARCUATE BUNDLES
- RAKED OR THINNED APPEARANCE
- STRIATIONS ARE LESS BRIGHT
- TEXTURE IS FINER
- TERTIARY VESSELS ARE VISIBLE
- COMPARE SUPERIOR TO INFERIOR
- LOOK FOR RIM THINNING OR NOTCH
- COMPARE RIGHT TO LEFT EYE
- REVERSAL MAY OCCUR
  - DIM / BRIGHT / DIM
NFL PEARLS

• LOOK AT THE NFL IN ALL PATIENTS
  • EVEN THE HEALTHY ONES
• NOT PATHOGNOMONIC FOR GLAUCOMA
  • WE LOSE NFL AS WE AGE
  • OTHER DISEASES CAUSE NFL LOSS AS WELL
• 60% HAVE VISIBLE NFL LOSS 4-6 YRS BEFORE VF LOSS
• CORRELATE NFL LOSS WITH ONH DAMAGE / VF LOSS
• PREDICT VISUAL FIELD LOSS WITH NFL EVALUATION
• USE SYMMETRY OF THE NFL FOR COMPARISON
  • COMPARE SUPERIOR / INFERIOR AND BETWEEN THE TWO EYES
• GLAUCOMA SUSPECTS WITH NFL ABNORMALITES
  • HAVE ALREADY BEGUN TO SUFFER EARLY DAMAGE AND SHOULD BE TREATED
QUESTION

THAT’S TOO HARD. CAN’T I JUST LET A MACHINE DO IT FOR ME?
ADVANCED ONH IMAGING DEVICES

- HRT, OCT, GDX
- ALL HAVE BEEN REVISED OVER THE YEARS
- SOME CAN DO MORE THAN JUST EVALUATE GLAUCOMA
- STUDIES HAVE SHOWN STRENGTHS / WEAKNESSES
PROBLEMS WITH ADVANCED ONH IMAGING

- NEED CLEAR MEDIA
- NEED GOOD FIXATION
- ARE OPERATOR DEPENDENT
  - MUST UNDERSTAND NEED FOR GOOD DATA
  - MUST BE WILLING TO EDUCATE, WORK WITH THE PATIENT
  - MUST CENTER THE OPTIC NERVE AND MAP IT IN THE HRT
  - MUST OBTAIN GOOD SIGNAL STRENGTH / QUALITY
    - OCT
      - STRATUS / CIRRUS > 5 IS AN ABSOLUTE MINIMUM, PREFER > 7
      - SPECTRALIS > 18 IS RECOMMENDED PER COMPANY REPS
        - ACTIVE TRACKING LOCKS THE IMAGE TO THE FUNDUS, INCREASED REPEATIBILITY
    - HRT
      - < 30 IS PREFERRED PER COMPANY REPS, < 40 HRT STILL REPORTS ACCEPTABLE
    - GDX
      - > 7 IS PREFERRED, CENTERED AND EVENLY ILLUMINATED
SUSPECTING GLAUCOMA USING THE OCT

From a review of the literature / clinical trials, this information applies to the Stratus (time domain) and Cirrus (spectral domain).

Based on clinical experience, this can be loosely applied to the Spectralis as well.

NFL average thickness outside 95% CI (yellow <5 % or red <1%)

OR

NFL thickness in 1 quadrant (sup / inf) outside 95% CI (yellow <5 % or red <1%)

OR

NFL thickness in at least 2 clock hours (not directly temporal and not counting anything nasally) outside 95% CI (yellow <5 % or red <1%)

OR

Asymmetry between the 2 eyes’ average thickness of > 9 um
ADVANCED IMAGING PEARLS

- OCT / HRT / GDX
  - BUY / USE BASED ON YOUR NEEDS
  - ALL MAY HELP WITH DIAGNOSIS AND MONITORING
- GANGLION CELL CONCENTRATION (NEW)
  - CONSIDER MEASURING THIS AS IT MAY SHOW DAMAGE PRIOR TO NFL LOSS AND PRIOR TO VISUAL FIELD LOSS, MAY BE ABLE TO MONITOR FOR PROGRESSION
- NEVER INTERPRET A SCAN BY ITSELF
  - ALWAYS CORRELATE ONH / NFL SCAN TO CLINICAL FINDINGS
- DATA FROM ONE MACHINE DOES NOT ALWAYS CORRELATE WITH ANOTHER MACHINE
  - STRATUS VS CIRRUS, OCT ONH VS HRT ONH, NFL: OCT/GDX/HRT
- THE MACHINE DOES NOT MAKE THE DIAGNOSIS
  - THE CLINICIAN GATHERS ALL THE APPROPRIATE DATA, PUTS IT ALL TOGETHER AND ULTIMATELY MAKES THE DIAGNOSIS
QUESTION

TRUE OR FALSE, IF THE NFL IS NORMAL AND THE VISUAL FIELD IS NORMAL, THE PATIENT HAS TO BE NORMAL?
A NORMAL VISUAL FIELD DOES NOT EXCLUDE GLAUCOMA

- NORMAL FIELD EXCLUDES ADVANCED DISEASE
  - BUT DOES NOT RULE IT OUT
  - DUE TO OVERLAP OF RECEPTOR SITES IN THE RETINA
- 20-40% OF RGC LOST BEFORE 5-10 DB VF REDUCTION
- SOME SHOW INNOCUOUS VF DESPITE GLAUCOMA
- VF WILL EVENTUALLY CATCH UP TO THE ONH
- IF NORMAL STANDARD AUTOMATED PERIMETRY (SAP) BUT STILL STRONGLY SUSPICIOUS ONH
  - CONSIDER ADDITIONAL VF TESTING
    - SWAP
    - FDT
ALTERNATIVE VISUAL FIELD
PEARLS

• EARLY DETECTION = EARLY INTERVENTION
  • CONSIDER SITA SWAP / FDT EARLY
    • IF PROGRESSION THEN SAP
  • CONSIDER WAITING FOR SAP DEFECT ONLY
• MOST PATIENTS PREFER SAP OVER SWAP
  • SWAP HAS GREATER VARIABILITY AND THERE IS A LEARNING CURVE
• MUST PICK PATIENTS WISELY
  • HIGH RISK SUSPECT, NORMAL SAP, GOOD VF TAKER
  • MINIMAL CATARACTS IF USING SWAP
• BOTTOMLINE
  • NO SINGLE FUNCTIONAL OR STRUCTURAL TEST IS THE GOLD STANDARD FOR DETECTING EARLY GLAUCOMA
QUESTION

WHICH PATIENTS SHOULD BE TREATED?
RISK FACTORS
POAG AND POAG SUSPECTS AAO PPP 2010

- INTRAOCULAR PRESSURE LEVEL
- OLDER AGE
- FAMILY HISTORY OF GLAUCOMA
- THINNER CORNEA
- AFRICAN ANCESTRY OR LATINO/HISPANIC ETHNICITY
- LOW OCULAR PERFUSION PRESSURE
- TYPE 2 DIABETES
- MYOPIA
- GENETIC MUTATIONS
- OTHERS
  - MIGRAINES, PERIPHERAL VASOSPASM, CARDIOVASCULAR DISEASE, HTN, LOWER SYSTOLIC AND DIASTOLIC BLOOD PRESSURE
THE GLAUCOMA RISK ESTIMATOR

- BASED ON
  - AGE
  - VERTICAL C/D RATIO
  - 3 IOP MEASUREMENTS PER EYE
  - 3 CCT MEASUREMENTS PER EYE
  - 2 VF PATTERN STANDARD DEVIATIONS USING
    - HUMPHREY FULL 30-2 OR 24-2
    - HUMPHREY SITA STANDARD 30-2 OR 24-2
    - LOSS VARIANCE FROM OCTOPUS 32-2

- METHODS
  - CONTINUOUS METHOD
    - ENTER ACTUAL DATA FOR THE PATIENT AGE AND EYE MEASUREMENTS
  - POINT SYSTEM
    - SELECT RANGE FOR AGE AND AVERAGE OF MULTIPLE MEASUREMENTS

[Image of the Glaucoma Risk Estimator tool]

http://ohts.wustl.edu/risk/index.html

OCULAR HYPERTENSION TREATMENT STUDY (OHTS)

Figure 1. The percentage of participants in the observation group who developed primary open-angle glaucoma (median follow-up, 72 months)

Figure 2. The percentage of participants in the observation group who developed primary open-angle glaucoma (median follow-up, 72 months)

RISK DETERMINATION PEARLS

- Start every comprehensive exam with the understanding that the patient is a glaucoma suspect until proven otherwise.
- Evaluate the patient’s risk factors.
- Treat those at greatest risk.
  - Advanced disease, monocular, fast progression, definite fam hx of vision loss from glaucoma.
- Other factors to consider prior to treatment.
  - Health, life expectancy.
  - Patient preferences.
- Glaucoma risk estimator’s utility?
  - Not sure of its place in clinical practice but not bad for teaching.
  - How much risk are you and/or the patient willing to take?
  - C/D and PSD are variables but these may indicate early glaucoma.
- Discuss the risks with the patient, involve them in the decision to treat vs monitor and document the discussion in chart.
QUESTION

SHOULD THE IOP BE LOWERED AND IF SO, HOW LOW SHOULD IT BE?
THE CASE FOR LOWERING THE IOP

- CNTGS
  - LOWERING IOP 30% REDUCES RISK OF VF PROGRESSION IN HIGH RISK PATIENTS

- AGIS
  - MODERATE TO SEVERE POAG PATIENTS
    - OPTIMAL IOP IS 12 mm Hg (52% REDUCTION) TO PREVENT VF PROGRESSION
      - HOWEVER, SOME STILL PROGRESSED

- CIGTS
  - NEWLY DIAGNOSED POAG / MILD DAMAGE
    - 37% IOP REDUCTION HAD NO NET VF PROGRESSION X 5 YRS

- OHTS
  - REDUCING IOP WAS EFFECTIVE IN DELAYING OR PREVENTING ONSET OF POAG IN PATIENTS WITH ELEVATED IOP / THIN CCT

- SCOTTISH GLAUCOMA TRIAL
  - TRAB LOWERED IOP MOR THAN MEDICINE, MEDICINE GROUP HAD MORE VF DETERIORATION THAN MEDICINE

- MOORFIELDS PRIMARY TREATMENT TRIAL
  - IOP LOWERING: TRAB > LASER > MEDICINE, MEDICINE HAD MORE VF DETERIORATION

- EARLY MANIFEST GLAUCOMA TRIAL
  - LOWERING IOP WITH MEDICINE AND TRAB SLOWED PROGRESSION OF OPTIC DISC AND VF DAMAGE
TARGET PRESSURE

- DEFINITION
  - RANGE OF IOPS (BELIEVED TO BE) ADEQUATE TO STOP PROGRESSIVE PRESSURE-INDUCED INJURY
- SET TARGET IOP BASED ON
  - HIGHEST IOP
  - AMOUNT OF OPTIC NERVE DAMAGE AND / OR VISUAL FIELD LOSS
- CONSIDER
  - AGE AND RACE
  - PROGRESSION
  - MONOCULAR STATUS
  - FAMILY HX
  - BURDEN (TREATMENT’S IMPACT ON QUALITY OF LIFE)
- BE READY TO MODIFY AS NEEDED
SET TARGET IOP BASED ON ONH OR VF DAMAGE?

ONH DAMAGE

VISUAL FIELD DAMAGE

• 20-30% REDUCTION (OC HTN / NTG / MILD)
  • 1-2 MEDICATIONS
• 30-40% REDUCTION (MODERATE - SEVERE)
  • 2 MEDICATIONS
  • POSSIBLY ALT / SLT, ORAL CAI
• 40-50% REDUCTION (SEVERE)
  • 2-3 MEDICATIONS
  • ALT / SLT, ORAL CAI
  • TRABECULECTOMY OR TUBE
  • EX-PRESS SHUNT
  • CYCLODESTRUCTIVE PROCEDURE

Hodapp E, Parrish RK, Anderson, DR.
St. Louis.
CLASSIFYING FIELD DEFECTS

From: Glaucoma Handbook, AB Litwak, Editor, Butterworth-Heinemann, 2001

• Mild
  • MD < -5 dB
  • AND PD: < 14 pts below 5% AND < 8 pts below 1%
  • AND no point in central 5 degrees < 20 dB

• Moderate
  • MD < -5 to -10 dB
  • OR PD: 14-28 pts below 5% OR 8-16 pts below 1%
  • OR central points in one hemifield between 10-20 dB

• Severe
  • MD > -10 dB
  • OR PD: > 28 pts below 5% OR > 16 pts below 1%
  • OR < 20 dB in both hemifields in central 5 degrees
  • OR any point in central 5 degrees < 10 dB
LOWERING THE IOP

- NOT AS EASY AS YOU MIGHT THINK
- NOT AS SIMPLE AS JUST GOING LOW
- PROBLEMS
  - IOP PEAKS IN THE MORNING
  - BLOOD PRESSURE BOTTOMS OUT IN THE MORNING
    - BALANCE BETWEEN IOP AND BLOOD PRESSURE
      - OCULAR PERFUSION PRESSURE
        - BALANCE IS NECESSARY TO SUSTAIN OPTIC NERVE
  - IOP CAN SPIKE AT ANY TIME
TARGET IOP PEARLS

- LOWERING TO “WITHIN NORMAL” NO LONGER AN ACCEPTABLE APPROACH
- SET TARGET BASED ON AMOUNT OF DAMAGE
  - VISUAL FIELD (MEAN DEVIATION AND CENTRAL PTS)
  - ONH APPEARANCE
  - NFL LOSS
  - **DEFER TO THE ONE WITH THE MOST DAMAGE**
- IF ABOVE TARGET OR PROGRESSION NOTED
  - RECOGNIZE IT AND BE PREPARED TO MODIFY TREATMENT ACCORDINGLY
QUESTION

WHEN TREATING OCULAR HTN OR GLAUCOMA, WHAT IS YOUR PREFERRED FIRST LINE AGENT?

1. PROSTAGLANDIN
2. NON-SELECTIVE BETA-BLOCKER
3. CARDIOSELECTIVE BETA-BLOCKER
4. ALPHA-AGONIST
5. TOPICAL CARBONIC ANHYDRASE INHIBITOR
6. MIOTICS
### Poll Result

When treating ocular hypertension or glaucoma, what is your preferred class for a first line agent?

1. Prostaglandin  
   - 96%
2. Non-selective beta blocker  
   - 2%
3. Cardioselective beta-blocker (Betaxolol)  
   - 1%
4. Alpha-Agonist (Brimonidine or Alphagan)  
   - 1%
5. Topical Carbonic Anyhydrase Inhibitor  
   - 0%
6. Miotics  
   - 0%
PROSTAGLANDINS

**OPTIONS**

- XALATAN (1996)
- RESCULA (2000) - DISCONTINUED
- LUMIGAN (2001)
- TRAVATAN (2001)
- TRAVATAN Z (2006)
- LATANOPROST 0.005% (2011)
- TAFLUPROST 0.0015% (2012)
PROSTAGLANDINS

• MECHANISM
  • ALL ENHANCE UVEOSCLERAL OUTFLOW
    • LUMIGAN MAY AID CONVENTIONAL TM OUTFLOW

• EFFICACY
  • 20-33% REDUCTION OF IOP
  • IOP REDUCTION STARTS IN 3-4 HOURS
  • MAXIMUM IOP EFFECT AFTER 8-12 HOURS
  • 24-36 HOUR DURATION OF EFFECT AND MAYBE EVEN LONGER

• DOSING
  • ONCE A DAY
    • IMPROVES COMPLIANCE / PERSISTENCE
PROSTAGLANDINS

- OCULAR SIDE EFFECTS
  - HYPEREMIA
  - SPK
  - LONGER / THICKER LASHES
  - IRIS COLOR CHANGES (MELANIN)
  - PERIOcular PIGMENTARY CHANGES
  - UVEITIS, CME 3-4%
  - HSK REACTIVATION

- SYSTEMIC SIDE EFFECTS
  - MUSCLE / JOINT PAIN, GI DISTRESS, SKIN RASH

- CONTRAINDICATIONS
  - UVEITIS, APHAKIA, AC/IOL, TORN POSTERIOR LENS CAPSULE, H/O HERPES SIMPLEX

- PREGNANCY / NURSING / CHILDREN
  - CATEGORY C, USE WITH CAUTION
IS THERE A DIFFERENCE?
IS THERE A DIFFERENCE?

IOP

HYPEREMIA

XLT STUDY
Parrish RK, ET AL. AJO. May 2003: 688-703
WHAT’S “NEW”?

- **PROSTAGLANDIN-ASSOCIATED PERIORBITOPATHY**
  - **SIGNS**
    - Deepening of superior lid sulcus
    - Ptosis
    - Enophthalmos
    - Involution of dermatochalasis
  - **MECHANISM**
    - Not completely understood
    - Theory
      - Smooth muscle contraction
      - Periorbital fat cell atrophy
  - **COSMESIS**
    - - Maybe avoid prostaglandins if unilateral tx
    - + Blepharoplasty in a bottle
      - Periorbital fat atrophy photo after 1 month
  - **EDUCATION**
    - Discuss with patients this possibility
    - Now listed on the product insert
      - “Deepening of eyelid sulcus”
      - Not an adverse effect as not in clinical trials
WHAT’S “NEW”?

- TAFLUPROST (ZIOPTAN™, MERCK)
  - MECHANISM
    - BELIEVED TO INCREASE UVEOSCLERAL OUTFLOW
    - EXACT MECHANISM IS UNKNOWN
  - IOP EFFECT
    - 20-33%, SIMILAR TO LATANOPROST IN 2 STUDIES
  - ADVERSE REACTIONS
    - PIGMENTATION, EYELASH CHANGES, INTRAOCULAR INFLAMMATION, MACULAR EDEMA
    - 4-20% CONJUNCTIVAL HYPEREMIA, 1% DISCONTINUED
  - STORAGE
    - REFRIGERATE UNOPENED POUCHES, ROOM TEMP OPENED FOR 28 DAYS
  - COST
    - $89.00 AT PHARMACYCHECKER.COM 8/11/12
    - COULD NOT FIND AT WALMART.COM, CVS ONLINE, WALGREENS ONLINE, COSTCO ONLINE
WHAT’S “NEW”?

• TAFLUPROST (ZIOPTAN™, MERCK)
  • BENEFITS
    • PRESERVATIVE FREE
      • TOXIC EFFECT OF PRESERVATIVES ON OCULAR SURFACE
        • CONJUNCTIVAL HYPEREMIA
        • CELLULAR APOPTOSIS
        • OCULAR SURFACE DISEASE
        • INFLAMMATORY CELL INFILTRATION OF CONJUNCTIVA
      • MECHANISM OF BAK DAMAGE IS UNKNOWN
    • LONGTERM TREATMENT WITH PRESERVATIVES MAY REDUCE THERAPEUTIC SUCCESS OF FILTRATION SURGERY
QUESTION

ARE GENERICS JUST AS GOOD?
GENERICS

- $80 BILLION INDUSTRY IN 2011
  - $74 BILLION IN 2010
  - ACCOUNTS FOR 80% OF 4 MILLION PRESCRIPTIONS IN US
- REDUCES MEDICATION PRICE DUE TO COMPETITION
- 3 MOS AFTER GENERIC ON MARKET, NAME BRAND LOSES 50% SHARE OF MARKET, 80% AT 1YR
- PATENTS LAST 20 YRS FROM FILING, EFFECTIVE LIFE IS REALLY ONLY A FEW YEARS
  - KEEP IN MIND
    - CLINICAL DEVELOPMENT OF 10-12 YEARS
    - $100-500 MILLION INVESTMENT
GENERIC IOP MEDS

- OPTIONS
  - BETA-BLOCKERS
    - TIMOLOL, LEVOBUNOLOL, CARTEOLOL, BETAXOLOL
  - ALPHA AGONISTS
    - BRIMONIDINE 0.15, 0.2
  - PARASYMPATHOMIMETICS
    - PILOCARPINE
  - FIXED COMBINATIONS
    - DORZOLAMIDE / TIMOLOL
  - PROSTAGLANDIN ANALOGUES
    - LATANOPROST
  - ORAL CARBONIC ANHYDRASE INHIBITORS
    - ACETAZOLAMIDE, METHAZOLAMIDE
GENERICS

• TO GET FDA APPROVAL
  • BE BIOEQUIVALENT
  • SAME ACTIVE INGREDIENT
  • IDENTICAL STRENGTH, DOSAGE FORM, LABELLING, INDICATIONS, ROUTE
  • SAME BATCH REQUIREMENTS
    • IDENTITY, STRENGTH, PURITY, QUALITY
  • SIMILAR SHELF LIFE
  • SAME MANUFACTURING PROCESS REGULATIONS
• GENERIC MANUFACTURERS DO NOT NEED TO REPEAT SAFETY AND EFFICACY STUDIES
GENERICS

• HOWEVER
  • NOT REQUIRED TO BE THERAPEUTICALLY EQUAL UPON RELEASE

• PROBLEM
  • DROP SIZES DIFFER (25-70 uL)
  • BOTTLE HARDER TO HANDLE, TOUGHER TO TELL WHEN NEED REFILLS, CLOGGED DROPPER, ETC.
    • MAY LEAD TO NONCOMPLIANCE

• RECENT STUDY OF 5 GENERIC FORMULATIONS OF LATANOPROST
  • DELIVERY DOSE CAN VARY BY 20%

• RECENT STUDY OF 3 GENERIC FORMULATIONS OF LATANOPROST
  • DIFFERENCES IN
    • VISCOSITY, PH, SPECIFIC GRAVITY, AMOUNT / NUMBER OF DROPS PER BOTTLE, MEAN DROP SIZE, MICROGRAMS OF ABSOLUTE DRUG PER DROP RECOMMENDATION
GENERICS

- $22.99 / 2.5 ml AT DRUGSTORE.COM 06/01/11
- 2007 LATANOPROST STUDY IN INDIA
  - 30 PATIENTS
  - 9/11 OAG PATIENTS HAD > 30% IOP REDUCTION VS 3/18 ON GENERIC
  - NAME BRAND IOP 37% LESS VS 25% GENERIC
  - SIMILAR SIDE EFFECTS
  - GENERIC HAD A HIGHER pH AND PARTICULATE MATTER
    - MAY AFFECT STABILITY AND RELEASE OF ACTIVE DRUG
- $4 / 30 DAY, $10 / 90 DAYS @ WALMART, ETC.
- 2002 TIMOLOL STUDY
  - NAME BRAND HAD LOWER IOP AT 8H COMPARED TO GENERIC
  - DIFFERENT FORMULATIONS = DIFFERENT SIDE EFFECTS
    - SORBATE > STINGING THAN HEMIHYDRATE / GFS
    - GFS > BLURRED / DIMMED VISION THAN HEMIHYDRATE OR SORBATE
TOPICAL TREATMENT PEARLS

• CONSIDER
  • EFFICACY
  • ABILITY TO FLATTEN THE DIURNAL CURVE
  • SAFETY
  • CONVENIENCE
  • COST

• PROSTAGLANDINS SHOULD BE FIRST-LINE EXCEPT FOR
  • ACUTE ANGLE CLOSURE GLAUCOMA
  • UVEITIC GLAUCOMA
  • NEOVASCULAR GLAUCOMA

• GENERICS
  • GOOD FOR COST BUT NOT NECESSARILY SAME IOP EFFECT
  • BE CAREFUL, TRIAL AND ERROR TO SEE HOW PATIENT DOES
  • CONSIDER WRITING DISPENSE AS WRITTEN ON RX

• THE ORANGE BOOK: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm
  • “A” – THERAPEUTICALLY EQUAL, NO KNOWN / SUSPECTED BIOEQUIVALENCE PROBLEMS
QUESTION

THE BEST WAY TO DETERMINE IF A PATIENT IS PROGRESSING IS…
DETECTING PROGRESSION

• ESTABLISHED METHODS
  • VISUAL FIELDS
    • IDENTIFYING PROGRESSION
      • NEW DEFECT, DEEPENING OF DEFECT, ENLARGEMENT / EXPANSION OF DEFECT
    • EVENT ANALYSIS (CHANGE FROM BASELINE)
      • LONGITUDINAL ASSESSMENT OF STANDARD AUTOMATED PERIMETRY
      • GLAUCOMA PROGRESSION ANALYSIS (NEED 3 VF, GPA: NO / POSSIBLE / LIKELY PROGRESSION)
    • TREND ANALYSIS (RATE OF CHANGE OVER TIME)
      • VISUAL FIELD INDEX (NEED 5 VF)
  • OPTIC NERVE APPEARANCE
    • CLINICAL EXAMINATION
    • OPTIC DISC / NFL PHOTOGRAPHY
• ADJUNCTIVE METHODS
  • ONH / NFL TESTING (OCT / GDX, HRT)
  • GANGLION CELL COMPLEX
    • DAMAGE POSSIBLE BEFORE SHOWS UP ON NFL / VISUAL FIELD / ONH
WHAT DO THE STUDIES SAY?

• OHTS
  • 55% PROGRESS BY DISC PHOTOS VS 35% PROGRESSED BY VF

• CNTGS
  • 89% PROGRESSED ON VF VS 11% PROGRESSED ON ONH PHOTOS

• CIGTS AND AGIS
  • USED 2 DIFFERENT METHODS TO DETERMINE VISUAL FIELD PROGRESSION
2012 VF STUDY
GPA VS EXPERT CONSENSUS

GPA = Glaucoma Progression Analysis
VF = Visual Field

100 EYES, 83 WITH GLAUCOMA
5 MASKED GLAUCOMA SPECIALISTS
5 SERIAL FIELDS
INITIAL EVALUATION OF VF BY SPECIALIST THEN AGAIN 4 MONTHS LATER WITH ACCESS TO GPA
RESULTS
FAIR AGREEMENT

Glaucoma Progression Analysis Software Compared with Expert Consensus Opinion in the Detection of Visual Field Progression in Glaucoma

Angelo P. Tenna, MD, Donald L. Buczkowski, MD, MPH, Jagadeesh Bandi, MD, MPH, William J. Feyer, MS, Robert M. Federman, MD, Leon W. Herndon, MD, Douglas J. Rhee, MD, Julia Whiteside-de Vos, MD, MPH, Joyce Huang, BA, Douglas R. Anderson, MD

Purpose: To compare the results of Glaucoma Progression Analysis (GPA; Carl Zeiss Meditec, Dublin, CA) to subjective expert consensus in the detection of glaucomatous visual field progression.

Design: Retrospective, observational case series.

Participants: We included 100 eyes of 83 glaucoma patients.

Methods: Five serial Humphrey visual fields from 100 eyes of 83 glaucoma patients were evaluated by 5 masked glaucoma subspecialists for determination of progression. Four months later, with a randomly reordered patient sequence, the same visual field series were reevaluated by the same graders, at which time they had access to the Glaucoma Progression Analysis (GPA) printout.

Main Outcome Measures: The level of agreement between majority expert consensus and GPA, both before and after access to GPA data, was assessed using kappa statistics.

Results: On initial review and on reevaluation with access to the GPA printout, the level of agreement between majority expert consensus and GPA was fair (kappa = 0.52, 95% confidence interval [CI]: 0.26–0.69 and kappa = 0.62, 95% CI, 0.46–0.75, respectively). Expert consensus was more likely to classify a series of fields as showing progression than was GPA (P<0.002). There was good agreement between expert consensus on initial review and reevaluation 4 months later (kappa = 0.77, 95% CI, 0.65–0.90).

Conclusions: The level of agreement between majority expert consensus of subjective determination of visual field progression and GPA is fair. In cases of disagreement with GPA, the expert consensus classification was usually progression. Access to the results of GPA did not significantly change the level of agreement between expert consensus and the GPA result; however, expert consensus did change in 11 of 100 cases.

Financial Disclosure: Proprietary or commercial disclosure may be found after the references.

2011 ADJUNCTIVE TESTING STUDY

- 2011 STUDY
  - 108 EYES OF 70 GLAUCOMA PATIENTS
  - FOLLOWED EVERY 4 MONTHS FOR 2.9 YEARS
  - 1105 OCT, 1062 HRT, 1099 VF MEASUREMENTS
- RESULTS
  - AGREEMENT WAS POOR
  - ONLY 1 EYE (0.9%) HAD PROGRESSION ON ALL 3
- CONCLUSION
  - DUE TO VARIABILITY IN THE NFL, ONH RIM, VFI, PROGRESSION SHOULD BE EVALUATED ON AN INDIVIDUAL BASIS
WGA CONSENSUS STATEMENTS

Progression of Glaucoma, World Glaucoma Association, 2011 Kugler Publications

- BOTH ONH STRUCTURE AND FUNCTION SHOULD BE EVALUATED FOR DETECTION OF PROGRESSION
- CURRENTLY, NO SPECIFIC TEST CAN BE REGARDED AS THE PERFECT STANDARD FOR DETERMINATION OF PROGRESSION
- ONCE THE DIAGNOSIS OF GLAUCOMA HAS BEEN MADE, THE MOST IMPORTANT REMAINING QUESTION IS WHETHER THE DISEASE IS STABLE AND THE THERAPY / COMPLIANCE ARE SUFFICIENT, OR WHETHER THE DISEASE IS PROGRESSIVE AND THE THERAPY IN RELATION TO THE LIFE EXPECTANCY HAS TO BE INTENSIFIED
- PROGRESSION DETECTED BY FUNCTIONAL MEANS WILL NOT ALWAYS BE CORROBORATED USING STRUCTURAL TESTS, AND VICE-VERSA
PROGRESSION PEARLS

• THE MOST DIFFICULT ASPECT OF MANAGING GLAUCOMA
• EVEN SPECIALISTS CANNOT AGREE ON BEST METHOD
• RECOMMENDATIONS
  • COMPARE SERIAL VISUAL FIELDS
    • IT IS DIFFICULT TO DIFFERENTIATE LONG TERM FLUCTUATION (CAN VARY BY 10 DB OR GREATER) FROM ACTUAL PROGRESSION
    • USE GLAUCOMA PROGRESSION ANALYSIS / VFI SOFTWARE
    • CONSIDER RECORDING INTERPRETATION OF PATTERN, MD, GPA, VFI
    • SWITCH TO 10-2 AND MACULA AS NEEDED
    • RE-ESTABLISH BASELINE: CHANGE IN TARGET OR THERAPY OR LAST 2 VF THAT SHOW PROGRESSION
  • COMPARE SERIAL ONH / NFL PHOTOS
    • CONSIDER RECORDING PHOTO REVIEW INTERPRETATION
  • COMPARE SERIAL GDX, OCT, HRT
    • USE SERIAL ANALYSIS SOFTWARE (OCT: GPA, HRT: TCA / TREND)
    • NO POINT IN MEASURING NFL AROUND 50 (NOISE BELOW THAT, ASTROCYTES, GLIAL TISSUE, BLOOD VESSELS)
    • CONSIDER GCC
  • REPEAT TESTING IF SUSPICIOUS
  • WHEN IN DOUBT, DISCUSS WITH PATIENT AND TAKE ACTION
QUESTION

WHY DID THIS PATIENT PROGRESS?
NONCOMPLIANCE

You Can Lead a Horse to Water...
NONCOMPLIANCE

- DEFINITION
  - THE INTENTIONAL OR ACCIDENTAL FAILURE TO COMPLY WITH A PHYSICIAN’S EXPRESSED OR IMPLIED DIRECTIONS WITH REGARD TO TAKING MEDICATIONS OR FUTURE APPOINTMENTS
- ONLY 27-59% OF PATIENTS FOLLOW INSTRUCTIONS
- 10% OF GLAUCOMA RELATED BLINDNESS HAS BEEN ATTRIBUTED TO PATIENT NONCOMPLIANCE
NEW TERMS

• ADHERENCE
  • THE MEASURE OF THE DEGREE TO WHICH PATIENT FOLLOWS PRESCRIBED INSTRUCTIONS DURING A TIME PERIOD
    • ALLOWS PATIENT TO HAVE LAPSES IN PERFECT DRUG TAKING, SUMMARIZES THE PERCENT OF DAYS ON WHICH THE PATIENT HAS DRUG TO USE

• PERSISTENCE
  • EVALUATES THE TIME UNTIL THE PATIENT FIRST DISCONTINUES USE OF A MEDICATION
    • A MEASURE OF TIME TO DISCONTINUATION
REASONS FOR NONCOMPLIANCE

- FORGETFULNESS
- INCONVENIENCE
- DOSING FREQUENCY
- DIFFICULTY GETTING APPT
- NOT CONSIDERED SERIOUS
- WAITING TIME IN CLINIC
- INABILITY TO INSTILL DROPS
- SIDE EFFECTS OF MEDICATION
- CONFUSING INSTRUCTIONS

- COST OF THERAPY
- NO IMPROVEMENT OF SYMPTOMS
- LACK OF TRANSPORTATION
- RAN OUT OF MEDICATIONS
- FEAR
- LACK OF INSURANCE
- TOO MANY MEDICATIONS
IMPROVING COMPLIANCE

- TIE THE DRUG TO A DAILY TASK
- TIMING SHOULD BE CONVENIENT FOR THE PATIENT
- USE FEWEST DROPS NECESSARY
- REVIEW INSTILLATION
- RECOMMEND MAIL ORDER
- MINIMIZE TREATMENT REGIMEN
- MINIMIZE INCONVENIENCE
- PREDICT SIDE-EFFECTS
- RECOMMEND COMPLIANCE AIDS
- WORK ON DOCTOR / PATIENT COMMUNICATION
SHARED RESPONSIBILITY

• DOCTOR’S ROLE
  • DOCTOR-PATIENT BOND STARTS FROM DAY 1
  • EDUCATE PATIENTS ABOUT THEIR DISEASE
  • EXPLAIN BENEFITS AND SIDE EFFECTS OF MEDICATIONS AND THERAPY
  • EXPLAIN OTHER TREATMENT OPTIONS
  • EMPHASIZE THE POSITIVE
  • DON’T IGNORE THE NEGATIVE
  • DEVELOP THE PATIENT’S TRUST

• PATIENT’S ROLE
  • SEEK MEDICAL ADVICE
  • KEEP APPOINTMENTS
  • ALLOW FOR DIAGNOSTIC INVESTIGATIONS
  • ADHERE TO MEDICAL AND SURGICAL REGIMENS
  • MUST TAKE ACTIVE ROLE IN THEIR HEALTH CARE
COMPLIANCE PEARLS

- Medications only work if your patient uses them
- If patient progresses, consider non-compliance as cause

How to Help

- Limit medications / regimen if possible
- Tie medication usage to daily task
- Discuss with the patient and consider taking next step

Educate patient about importance of

- Compliance with medications / appointments
  - Consider the following as part of education template
    - Educated pt of the findings, the patient’s risk factors for glaucoma and the risk of irreversible blindness from glaucoma. Discussed the long-term nature of treatment and the importance of attending follow-up visits despite the ongoing use of medications and lack of visual symptoms.
  - Enter no show notes and orders to re-schedule and for patient to be notified of re-scheduled appointment
QUESTION

SINCE THE PATIENT IS PROGRESSING, WHAT’S THE NEXT STEP?
SECOND-LINE TREATMENT OPTIONS

- OHTS AND CIGTS
  - 2 IOP MEDICATIONS REQUIRED TO REACH TARGET
- OPTIONS
  - CHANGE WITHIN CLASS OF TOPICAL MEDICATION
  - CHANGE TO A DIFFERENT CLASS OF TOPICAL MEDICATION
  - ADD A MEDICATION
    - TOPICAL SINGLE
    - TOPICAL COMBINATION
    - ORAL
  - LASER TRABECULOPLASTY (ALT OR SLT)
- SURGERY
  - TRABECULECTOMY / TUBE / EX-PRESS SHUNT / CYCLODESTRUCTION
WHAT TO ADD TO A PROSTAGLANDIN?

**TABLE 1**

### PG Adjunctive Therapies Comparative Studies: Alpha-adrenergic Agonists versus Other Agents

<table>
<thead>
<tr>
<th>Reference</th>
<th>Comparing Agent</th>
<th>Comparing Agent B</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>O'Connor et al [2002]</td>
<td>brimonidine + latanoprost</td>
<td>dorzolamide + latanoprost</td>
<td>A &lt; B</td>
</tr>
<tr>
<td>Erdogan et al [2003]</td>
<td>brimonidine tartrate + latanoprost</td>
<td>latanoprost + placebo</td>
<td>A &gt; B</td>
</tr>
<tr>
<td>Stewart et al [2004]</td>
<td>brimonidine tartrate + latanoprost</td>
<td>latanoprost/timolol (morning dose)/FC</td>
<td>equal efficacy</td>
</tr>
<tr>
<td>Konstas et al [2005]</td>
<td>brimonidine purite + latanoprost</td>
<td>dorzolamide + latanoprost</td>
<td>equal efficacy</td>
</tr>
<tr>
<td>Reis et al [2006]</td>
<td>brimonidine tartrate + travoprost</td>
<td>brinzolamide + travoprost</td>
<td>A &lt; B</td>
</tr>
<tr>
<td>Reis et al [2006]</td>
<td>brimonidine tartrate + travoprost</td>
<td>timolol + travoprost</td>
<td>A &lt; B</td>
</tr>
<tr>
<td>Feldman et al [2007]</td>
<td>brimonidine purite + travoprost</td>
<td>timolol + travoprost</td>
<td>A &lt; B</td>
</tr>
</tbody>
</table>

**TABLE 2**

### PG Adjunctive Therapies Comparative Studies: Topical Carbonic Anhydrase Inhibitors versus Other Agents

<table>
<thead>
<tr>
<th>Reference</th>
<th>Comparing Agent A</th>
<th>Comparing Agent B</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>O'Connor et al [2002]</td>
<td>dorzolamide + latanoprost</td>
<td>timolol + latanoprost</td>
<td>A &gt; B (small retrospective clinical trial)</td>
</tr>
<tr>
<td>Tamer et al [2007]</td>
<td>dorzolamide + latanoprost</td>
<td>timolol + latanoprost</td>
<td>A &gt; B</td>
</tr>
<tr>
<td>Konstas et al [2005]</td>
<td>dorzolamide + latanoprost</td>
<td>brimonidine purite + latanoprost</td>
<td>equal efficacy</td>
</tr>
<tr>
<td>Maruyama et al [2006]</td>
<td>dorzolamide + latanoprost</td>
<td>carteol + latanoprost</td>
<td>equal efficacy</td>
</tr>
<tr>
<td>Reis et al [2006]</td>
<td>brinzolamide + travoprost</td>
<td>brimonidine tartrate + travoprost</td>
<td>A &gt; B</td>
</tr>
<tr>
<td>Hollo et al [2006]</td>
<td>brinzolamide + travoprost</td>
<td>timolol + travoprost</td>
<td>equal efficacy</td>
</tr>
<tr>
<td>Tsukamoto et al [2006]</td>
<td>dorzolamide + (latanoprost + timol)/FC</td>
<td>brinzolamide + (latanoprost + timol)/FC</td>
<td>equal efficacy</td>
</tr>
</tbody>
</table>

PG = prostaglandins; FC = fixed combination. Eye-drops concentrations: latanoprost 0.005%, timolol 0.5%, dorzolamide 2%, brinzolamide 0.1%, brimonidine 0.2%, travoprost 0.004%, bimatoprost 0.03%.

PG = prostaglandins; FC = fixed combination; BB = betablocker. Eye-drops concentrations: latanoprost 0.005%, timolol 0.5%, dorzolamide 2%, brinzolamide 0.1%, brimonidine 0.2%, travoprost 0.004%, bimatoprost 0.03%.

PROBLEMS WITH LONG TERM MEDICAL THERAPY

• POOR ADHERENCE WITH MEDICATION USAGE
• SIDE EFFECTS FROM GLAUCOMA MEDICATIONS
• WIDE FLUCTUATIONS IN IOP DUE TO TROUGH EFFECTS AND DUE TO NOT USING MEDICATION AT APPROPRIATE TIMES
• REDUCED PROGNOSIS OF GLAUCOMA SURGERY DUE TO OCULAR SURFACE DISEASE
LASER TRABECULOPLASTY

• 1993 SURVEY OF AMERICAN GLAUCOMA SOCIETY
  • 92.9% NEVER / RARELY USED ALT AS INITIAL THERAPY
• USED AS ADJUNCTIVE THERAPY WHEN ON 2-3 MEDS
• SHOULD BE CONSIDERED FOR
  • NON-COMPLIANT PATIENTS
  • MEDICATION INEFFECTIVENESS / CONTRAINDICATIONS
  • UNABLE TO INSTILL MEDICATIONS
  • CANNOT AFFORD MEDICATIONS
  • PSEUDOEFOXOFLIATIVE GLAUCOMA
  • PIGMENTARY GLAUCOMA
  • PRIMARY OPEN-ANGLE GLAUCOMA
ALT VS SLT
SLT IN CLINICAL TRIALS

- COMPARED TO ALT
  - PROSPECTIVE, RANDOMIZED CLINICAL TRIAL = SIMILAR EFFECT

- EFFECT
  - IOP DECREASES 22-28% AFTER 36-49 WEEKS

- MAX MEDS, FAILED ALT
  - 70% RESPOND WITH > 3 MM HG DROP IN IOP
  - 24% SHOWED POST-OP IOP SPIKE > 5 mm Hg

- SLT COMPARED TO MEDICATION
  - SLT MED STUDY (PROSPECTIVE, RANDOMIZED, DOUBLE-ARM, 17 CTRS, 94 EYES)
    - SLT (58 EYES)
      - 100 APPLICATIONS, 360 DEGREES (REPEATED IF ABOVE TARGET)
    - MEDICATION (36 EYES)
      - MED CHANGED IF ABOVE TARGET, MORE STEPS NECESSARY TO ACHIEVE TARGET
  - RESULTS
    - SLT LOWERED IOP 26.4% VS 27.8% WITH MEDICINE AT 1YR
    - ? LONGTERM EFFECT

- CANADIAN AND US STUDY SAY SLT MAY BE MORE COST EFFECTIVE
QUESTION

WHEN SHOULD I SEND THE PATIENT FOR SURGERY?
INDICATIONS FOR SURGERY

- RARELY DONE AS INITIAL TREATMENT OPTION
- TYPICALLY DONE
  - WHEN MAXIMUM MEDICAL THERAPY AND LASER IS NOT SUFFICIENT TO CONTROL THE DISEASE
  - FOR DOCUMENTED PROGRESSION
  - WHEN MEDICATION CANNOT BE TOLERATED
  - WHEN COMPLIANCE CANNOT BE ACHIEVED
- HAVE TO CALCULATE RISK / BENEFIT RATIO
AGIS 7
Sustained IOP below 18 mm Hg:
Positive Correlation with Stability of Visual Field

Percent of Visits with IOP Less Than 18 mm Hg

Mean change in visual defect score

Follow-up (years)

GLAUCOMA SURGERY

TRABECULECTOMY

TUBE

Tube shunt device implanted in eye
TUBE VS TRAB (TVT) STUDY

• PROSPECTIVE STUDY (17 CENTERS, 212 EYES OF 212 PATIENTS)
  • 107 IN TUBE GROUP, 105 IN TRAB / MMC GROUP
  • PATIENTS (NOT “FRESH EYES”)
    • UNCONTROLLED GLAUCOMA, S/P CE/IOL AND / OR FAILED TRAB
  • 5 YEAR RESULTS (GEDDE SJ, ET AL. MARCH 3, 2011 AGS MEETING, CALIFORNIA)
    • IOP: 14.2 +/- 6.3mmHg TUBE VS 12.8 +/- 5.8 mmHg TRAB
    • PROBABILITY FAILURE: 26% TUBE VS 45% TRAB (P = 0.002)
    • LATE COMPLICATIONS: 34% TUBE VS 37% TRAB (P = .67)
    • ENDOPHTHALMITIS / BLEBITIS: TUBE 0 VS TRAB 4.8%
  • CONCLUSIONS
    • TUBE SHUNTS ARE A GOOD ALTERNATIVE IN THOSE WHO HAVE HAD PRIOR SURGERY
    • TOTAL COSTS OF TUBE WERE HIGHER THAN TRAB
    • NOT SURE OF WHICH IS BEST IN PRISTINE PATIENTS
WHAT’S “NEW” IN SURGERY

• OUTFLOW PROCEDURES
  • NEW OUTFLOW CHANNELS
    • OPTIONS: EX-PRESS GLAUCOMA IMPLANT
      • GOAL: EQUAL OR SURPASS EFFICACY / SAFETY OF STANDARD SURGERIES WITH LESS COMPLICATIONS
  • AUGMENT CONVENTIONAL OUTFLOW
    • OPTIONS: GONIOTOMY, TRABECTOME, CANALOPLASTY, ELT, MICRO-BYPASS STENT
      • GOAL: DECREASE DEPENDENCE ON GLAUCOMA MEDS AND ELIMINATE COMPLICATIONS DUE TO NO EXTERNAL BLEB
  • INCREASE UVEOSCLERAL OUTFLOW
    • OPTIONS: SOLX GOLD SHUNT
      • GOAL: SAME AS ABOVE
Ex-PRESS SHUNT

- FDA APPROVED 2003 (ALCON)
- PROCEDURE
  - STAINLESS STEEL, 3 MM IN SIZE, 50 UM TUBE
  - PRELOADED INSERTION DEVICE
  - IMPLANTED UNDER SCLERAL FLAP
  - DRAINS AQUEOUS FROM A/C INTO SUBCONJ
  -Creates A BLEB
Ex-PRESS (MINI) SHUNT

- **PROS**
  - NO IRIDECTOMY NEEDED, REDUCED INFLAMMATION AND HYPHEMA, DECREASED SURGICAL TIME, LESS HYPOTONY DUE TO CONSTANT LUMEN

- **CONS**
  - HAVE TO LEARN HOW TO DO IT, FOREIGN BODY MAY EXTRUDE, MORE EXPENSIVE?

- **USES**
  - ALTERNATIVE TO PRIMARY PROCEDURE (TRAB), APHAKIA, UVEITIC GLAUCOMA, PSEUDOPHAKIA

- **STUDY RESULTS**
  - LIMITED STUDY DATA
  - APRIL 2011
    - 39 EYES SHUNT VS 39 EYES TRAB
    - WHO STILL NEEDED MEDICATIONS?
      - 1YR 12.8% SHUNT VS 35.9% AFTER TRAB
      - 5YRS 41% SHUNT VS 53.9% AFTER TRAB
  - MORE / LARGER STUDIES ARE NEEDED
EX-PRESS VS TRABECULECTOMY

• EX-PRESS
  • NO IRIDECTOMY
  • PLACED UNDER SCLERAL FLAP
• 2011 STUDY
  • DUKE UNIVERSITY
  • 76 EYES EX-PRESS, 77 TRABECULECTOMY
• RESULTS
  • IOP ABOUT THE SAME
  • HYPOTONY
    • 4% EX-PRESS, 16% TRAB
  • MEDICATION REDUCTION
    • 87% EX-PRESS, 81% TRAB
2\textsuperscript{nd} / 3\textsuperscript{rd} Line Treatment Pearls

• MAXIMIZE MEDICAL THERAPY OR REFER FOR LASER
  • OR TREAT TO YOUR COMFORT LEVEL
• WHAT TO ADD TO PROSTAGLANDIN?
  • TOPICAL CAIS, THEN BETA-BLOCKER, THEN ALPHA AGONIST
• COMBINATIONS
  • LOWER IOP
  • INCREASE COMPLIANCE
  • MAY HELP WITH COST IF PATIENTS HAVE A CO-PAY
• LASER
  • ALT / SLT WORK EQUALLY WELL
  • SLT LESS DESTRUCTIVE, MAY BE ABLE TO BE REPEATED
• SURGERY
  • TRABS / TUBES BOTH WORK WELL BY SKILLED SURGEONS
  • EX-PRESS SHUNT AS EFFICACIOUS AS A TRAB
QUESTION

HOW DOES ALL OF THIS IMPACT THE PATIENT’S QUALITY OF LIFE?
QUALITY OF LIFE

WHAT IS IT?

DIFFICULT TO DEFINE AND EVEN HARDER TO MEASURE
- MASSOF RW AND RUBIN GS

VARIOUS DEFINITIONS
- AN INDIVIDUAL’S PERCEPTION OF THEIR POSITION IN LIFE IN THE CONTEXT OF CULTURE AND VALUE SYSTEMS IN WHICH THEY LIVE AND IN RELATION TO THEIR GOALS, EXPECTATIONS, STANDARDS AND CONCERNS
  - WORLD HEALTH ORGANIZATION
- PATIENT’S ABILITY TO ENJOY LIFE’S NORMAL ACTIVITIES
  - MEDICINE.NET
- A PERSON OR GROUP’S PERCEIVED PHYSICAL AND MENTAL HEALTH OVER TIME
  - CDC.GOV/HRQO
DOCTORS

• RELY ON MEASUREMENTS
  • INTRAOCULAR PRESSURE
  • VISUAL ACUITY
  • VISUAL FIELDS
  • OPTIC NERVE / NERVE FIBER LAYER

• PRIMARY CONCERN
  • FUNCTIONAL CAPABILITIES AND EFFICACY OF TREATMENT
PATIENTS

- **ARE NOT INTERESTED IN CLINICAL FINDINGS**
  - INTRAOCULAR PRESSURE
  - OPTIC NERVE / NERVE FIBER LAYER
  - VISUAL FIELD

- **THEY ARE INTERESTED IN THEIR QUALITY OF LIFE**
  - SPECIFICALLY
    - HOW COMFORTABLE THEY ARE
    - HOW WELL THEY SEE
GLAUCOMA PATIENTS

- QUALITY OF LIFE MAY BE IMPACTED BY
  - DIAGNOSIS
    - COMPREHENSION
    - PSYCHOLOGICAL RAMIFICATIONS (DISTRESS)
  - FUNCTIONAL LOSS
    - VISUAL ACUITY (MONOCULAR, BINOCULAR)
    - VISUAL FIELD (MONOCULAR, BINOCULAR)
    - COLOR / CONTRAST
    - INDEPENDENCE
  - TREATMENT
    - INCONVENIENCE
    - SIDE EFFECTS
    - COSTS
    - VISITS
GQL-15 STUDY RESULTS

- 2009 AUSTRALIA STUDY
- 121 GLAUCOMA, 31 CONTROLS
- INTERNAL GSS AND SEPARATE BPEI CRITERIA FOR SEVERITY CLASSIFICATION
  - EARLY / MILD -0.01 TO -6.00
  - MODERATE -6.01 TO -12.00
  - SEVERE -12.01
- GQL CORRELATED WITH
  - VISUAL ACUITY
  - VISUAL FIELD
  - DISEASE SEVERITY
- RESULTS
  - GLAUCOMA PATIENTS HAD POORER QUALITY OF LIFE
  - GLARE AND DARK ADAPTATION WERE MOST DISABLING

PSYCHOLOGICAL IMPACT

• THE DIAGNOSIS ALONE HAS RAMIFICATIONS

• FEAR OF BLINDNESS
  • NORWEGIAN STUDY (ODBERG ET AL. 2001)
    • 589 PATIENTS WITH GLAUCOMA
    • > 80% REPORTED NEGATIVE EMOTIONS AT TIME OF DIAGNOSIS
    • 1/3 HAD A FEAR OF BLINDNESS
  • CIGTS (JANZ NK ET AL. 2007)
    • 607 PATIENTS NEWLY DIAGNOSED WITH OPEN-ANGLE GLAUCOMA
    • 34% REPORTED A MODERATE AMOUNT OF FEAR OF BLINDNESS
      • 15% AT 1 YEAR, 12% STILL HAD FEAR AT 5 YEARS

• ANXIETY
  • 2002 FRENCH STUDY (HAMELIN N, ET AL. J FR OPHTHALMOL 2002)
    • 200 PATIENTS (MOST PATIENTS HAD GLAUCOMA)
  • RESULTS
    • ANXIETY LEAD TO PRESCRIPTION OF MINOR TRANQUILIZERS / ANTIDEPRESSANTS IN 11%
QUALITY OF LIFE PEARLS

- PATIENTS WORRY ABOUT
  - HOW WELL THEY SEE
  - HOW COMFORTABLE THEY ARE
- THE WORDS WE SAY MAY HAVE PSYCHOLOGICAL RAMIFICATIONS THAT IMPACT QUALITY OF LIFE
  - MAY NOT LAST BUT LONG BUT STILL WORRISOME
- AS GLAUCOMA WORSENS, QUALITY OF LIFE DECREASES
  - DUE TO VISION PROBLEMS
- GOAL OF TREATMENT
  - TO SLOW OR HALT PROGRESSION OF DISEASE
  - PRESERVE VISUAL FUNCTION THROUGHOUT PATIENT’S LIFE
CONCLUSIONS

- IOP AND CCT ARE RISK FACTORS FOR GLAUCOMA
- GLAUCOMA IS A DISEASE OF THE ONH
  - EVALUATE C/D WITH THE DISC SIZE IN MIND
  - LOOK FOR OTHER OPTIC NERVE HEAD SIGNS OF GLAUCOMATOUS DAMAGE
  - EVALUATE THE NERVE FIBER LAYER
  - USE ADVANCED ONH TESTING AS NEEDED
- EVALUATE THE VISUAL FIELD
  - CONSIDER ALTERNATIVES FOR EARLY DETECTION
- WEIGH / CALCULATE THE RISK
- MONITOR OR TREAT
  - TREAT PRE-PERIMETRIC GLAUCOMA IF NEEDED, SET A TARGET IOP, WATCH FOR PROGRESSION, MAXIMIZE THERAPY, REFER FOR LASER / SURGERY AS NEEDED
- MONITOR AND IMPROVE COMPLIANCE
- ALWAYS KEEP THE PATIENT’S QUALITY OF LIFE IN MIND