CONTROVERSIES IN GLAUCOMA

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QUESTION: IS ONE IOP ENOUGH?

INTRAOCULAR PRESSURE

- BALTIMORE EYE SURVEY (1991)
- DOCTORS WENT OUT INTO COMMUNITY AND DID COMPREHENSIVE EYE EXAMS
- 5308 BLACK AND WHITE PATIENT > 40 YEARS OLD
- GLAUCOMA DIAGNOSED BASED ON
- OPTIC NERVE AND VISUAL FIELD
- RESULTS
  - 55% HAD INITIAL IOP < 22 mmHg
  - 24% < 22 mmHg ON TWO READINGS
  - 16% < 22 mmHg ON THREE READINGS

IOP PEARLS

QUESTION: IS PACHYMETRY JUST AN IOP FIX OR IS IT SOMETHING MORE?

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 TREATMENT
    - TREAT THOSE AT GREATEST RISK
  - CCT
    - INFLUENCES GOLDMANN TONOMETRY
    - THICKNESS < 555 um HAVE 3X RISK COMPARED TO > 588

PACHYMETRY ADJUSTMENTS

- RACIAL VARIATIONS ARE PRESENT
  - CAUCASIAN 556 um
  - LATINO 546 um
  - AFRICAN AMERICAN 534 um
- NOMOGRAMS DO NOT AGREE
  - THINK: THIN / NORMAL / THICK
- ERRORS CAN OCCUR IF OFF AXIS
  - WATCH / TRAIN YOUR TECHNICIANS
- CONSIDER REPEATING ANOMALOUS READINGS UNTIL CONSISTENCY IS ESTABLISHED

CCT PEARLS

QUESTION: TRUE OR FALSE, YOU CAN TELL A PATIENT HAS GLAUCOMA BY THE C/D?

CUP / DISC RATIO

- NO LINE SEPARATES NORMAL FROM GLAUCOMA
- NORMAL VERTICAL C/D RATIO VARIES FROM 0.00-0.85
- C/D RATIO OF ≥ 0.65 OCCURS IN 2.2 - 4% OF NORMALS
- IT IS A FUNCTION OF DISC DIAMETER

HOW TO MEASURE OPTIC DISC DIAMETER

WHAT ELSE TO LOOK FOR: GLAUCOMATOUS 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
- NORMAL EYES
  - INFERIOR RIM > SUPERIOR > NASAL > TEMPORAL
- GLAUCOMA VIOLATES THE RULE (USUALLY)
    - 66 NORMAL EYES, 43 WITH OAG
    - HOWEVER, ISNT RULE INTACT IN 79% OF NORMALS VS 28% OF OAG (P<0.001)

C/D RATIO / ONH PEARLS

QUESTION: HOW DO I KNOW IF IT IS A GLAUCOMATOUS VISUAL FIELD?

VISUAL FIELDS
- FIELD LOSS IS AN INDICATOR OF ADVANCED DISEASE
- EARLY IN DISEASE
  - FOLLOW OPTIC NERVE CHANGES
- LATE IN DISEASE
  - FOLLOW VISUAL FIELD CHANGES
  - CONSIDER 10-2 AND MACULA
- GLAUCOMATOUS VF DEFECTS
  - THE ARCUATE DEFECT
  - THE NASAL STEP
  - THE PARACENTRAL DEFECT
  - DIFFUSE VISUAL FIELD LOSS

MINIMUM DIAGNOSTIC CRITERIA

QUESTION: WHAT IF THE VISUAL FIELD IS NOT WHAT YOU WERE EXPECTING?

VISUAL FIELD PEARLS

QUESTION: CAN YOU HAVE A NORMAL VISUAL FIELD AND STILL HAVE GLAUCOMA?

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

NFL EVALUATION

GLAUCOMA
- 60% HAVE VISIBLE NFL LOSS BEFORE VF LOSS BY UP TO 4-6 YRS
- 88% EYES THAT DEVELOP VF LOSS HAVE NFL DEFECTS
- NFL DEFECT CORRELATES WITH LOCATION OF VF LOSS
- DEFECTS MORE FREQUENT WITH ESTABLISHED VF LOSS
NORMAL NFL FEATURES
- FINE WHITE LINEAR STRIATIONS
- IN ANTERIOR RETINAL LAYER
- BRIGHT STRIATIONS WITH A FULMINANT, COARSE TEXTURE
- CASTS 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

NFL SLIT DEFECT
NFL WEDGE DEFECT
NFL DIFFUSE LOSS

NFL PEARLS

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
  - MUST OBTAIN GOOD SIGNAL STRENGTH / QUALITY
    - OCT
      - 5 IS AN ABSOLUTE MINIMUM
      - PREFER > 7
    - HRT
      - < 30 IS ACCEPTABLE

ADVANCED IMAGING PEARLS

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 BUT STILL STRONGLY SUSPICIOUS ONH
  - CONSIDER FDT AND / OR SWAP!

SHORT WAVE-LENGTH AUTOMATED PERIMATRY (SWAP)
- P-CELLS ARE THOUGHT FIRST DAMAGED IN GLAUCOMA
- SPARSE POPULATION OF P-CELLS INHIBITS MASKING OF DAMAGE DUE TO REDUNDANCY
- YELLOW DESENSITIZES RED AND GREEN CONES
BLUE CONES AND GANGLION CELL CONNECTIONS ARE TESTED
83% GLAUCOMA PTS HAVE SWAP DEFECT (3-5 YRS) BEFORE SAP
CORRELATES WITH NFL DAMAGE

SWAP PEARLS

QUESTION: WHICH PATIENTS SHOULD BE TREATED?

GLAUCOMA RISK FACTORS

GLAUCOMA RISK CALCULATOR

- 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

RISK DETERMINATION PEARLS

QUESTION: HOW LOW SHOULD YOU GO?

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

THE CASE FOR LOWERING THE IOP

- AGIS (MODERATE TO SEVERE POAG PATIENTS)
  - OPTIMAL IOP IS 12 mm Hg (52% REDUCTION) TO PREVENT VF PROGRESSION
- CIGTS (NEWLY DIAGNOSED POAG / MILD DAMAGE)
  - 37% IOP REDUCTION HAD NO NET VF PROGRESSION X 5 YRS
- CNTGS
  - 30% IOP REDUCTION REDUCES RISK OF VF PROGRESSION IN HIGH RISK PATIENTS
- OHTS
  - REDUCING IOP WAS EFFECTIVE IN DELAYING OR PREVENTING ONSET OF POAG IN PATIENTS WITH ELEVATED IOP / THIN CCT

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
TARGET IOP BASED ON ONH DAMAGE

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

TARGET IOP BASED ON VISUAL FIELD

- 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 / SHUNT
  - CYCLODESTRUCTIVE PROCEDURE

TARGET IOP PEARLS

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

PROSTAGLANDINS

QUESTION: WHAT ABOUT GENERICS?

TO GET FDA APPROVAL

- SAME ACTIVE INGREDIENT
- IDENTICAL STRENGTH, DOSAGE FORM, ROUTE
- SAME INDICATION FOR USAGE
- BE BIOEQUIVALENT
- SAME BATCH REQUIREMENTS
  - IDENTITY, STRENGTH, PURITY, QUALITY
- SIMILAR SHELF LIFE
- SAME MANUFACTURING PROCESS REGULATIONS

GENERICS
NOT REQUIRED TO BE THERAPEUTICALLY EQUAL UPON RELEASE

TIMOPTIC XE VS GENERIC
  o STATISTICALLY DIFFERENT IN IOP LOWERING AT 16 HRS
  o NAME BRAND HAD BETTER EFFICACY AND TOLERABILITY

DROP SIZES DIFFER, BOTTLE HARDER TO HANDLE, TOUGHER TO TELL WHEN NEED REFILLS, CLOGGED DROPPER, ETC.
  o MAY LEAD TO NONCOMPLIANCE

RECOMMENDATION
  o BE CAREFUL, TRIAL AND ERROR TO SEE HOW PATIENT DOES
  o CONSIDER WRITING "DISPENSE AS WRITTEN" ON RX

1ST LINE TREATMENT PEARLS

QUESTION: WHAT’S THE BEST WAY TO DETERMINE IF PROGRESSION HAS OCCURRED?

DETECTING GLAUCOMA PROGRESSION

- ESTABLISHED METHODS
  o VISUAL FIELDS
    ▪ LONGITUDINAL ASSESSMENT OF STANDARD AUTOMATED PERIMETRY
  o OPTIC NERVE APPEARANCE
    ▪ CLINICAL EXAMINATION
  o OPTIC DISC PHOTOGRAPHY

- ADJUNCTIVE METHODS
  o ONH / NFL ANCILLARY TESTING
    ▪ OCT, HRT, GDX, ETC.

NO CLEAR ANSWER AS TO BEST WAY TO MONITOR PROGRESSION

- OHTS
  o 55% PROGRESS BY DISC PHOTOS
  o 35% PROGRESS BY VF

- CNTGS
  o 89% PROGRESSED ON VF
  o 11% PROGRESSED ON ONH PHOTOS

- CIGTS AND AGIS
  o 2 DIFFERENT METHODS USED TO DETERMINE VISUAL FIELD PROGRESSION

SO WHICH METHOD IS BEST?

PROGRESSION PEARLS

QUESTION: WHY DID THIS PATIENT PROGRESS?

NONCOMPLIANCE

- DEFINITION
  o 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

- NONCOMPLIANT PATIENTS
  o HAVE LOWER LEVEL OF EDUCATION
  o ATTITUDE ABOUT DISEASE

REASONS FOR NONCOMPLIANCE

- DOCTOR’S ROLE
  o DOCTOR-PATIENT BOND STARTS FROM DAY 1
  o EDUCATE PATIENTS ABOUT THEIR DISEASE
  o EXPLAIN BENEFITS AND SIDE EFFECTS OF MEDICATIONS AND THERAPY
  o EXPLAIN OTHER TREATMENT OPTIONS
  o EMPHASIZE THE POSITIVE
  o DON’T IGNORE THE NEGATIVE
PATIENT’S ROLE
- Seek Medical Advice
- Keep Appointments
- Allow for Diagnostic Investigations
- Adhere to Medical and Surgical Regimens
- Patients Must Take Active Role

COMPLIANCE PEARLS

QUESTION: Since the patient is progressing, what do you do now?

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 Trabecuoplasty
  - Surgery
    - Trabeculectomy / Tube / Cyclodestruction

LASER TRABECULOPLASTY
- Survey of American Glaucoma Society
  - 92.9% Never / Rarely Use 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
  - Pseudoexfoliative Glaucoma
  - Pigmentary Glaucoma
  - Primary Open-angle Glaucoma

INDICATIONS FOR SURGERY
- Rarely Done as Initial Treatment Option
- 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

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

2ND / 3RD LINE TREATMENT PEARLS

QUESTION: ISN’T THERE ANYTHING THAT CAN PROTECT THE NERVE?

NEUROPROTECTION
  • “THE HOLY GRAIL”
  • WHAT IS IT
    ▪ INCREASE OF NEURONAL SURVIVAL FACTORS (RETINAL BASIC FIBROBLAST GROWTH FACTOR) PROTECTS PHOTORECEPTORS
  • RESULTS
    ▪ STUDIES HAVE BEEN WITH BRIMONIDINE ON RATS WITH CRUSH INJURIES
    ▪ NO EVIDENCE OF SIMILAR EFFECT IN HUMAN CLINICAL TRIALS
    ▪ ORAL CALCIUM CHANNEL BLOCKER, MEMANTINE, FAILED TO SHOW BENEFIT

QUESTION: HAS THIS PATIENT’S QUALITY OF LIFE BEEN IMPACTED?

DOCTORS
  • RELY ON OBJECTIVE MEASUREMENTS

PATIENTS
  • ARE NOT INTERESTED IN CLINICAL FINDINGS
  • THEY ARE INTERESTED IN THEIR QUALITY OF LIFE
    ▪ SPECIFICALLY
      ▪ HOW COMFORTABLE THEY ARE
      ▪ HOW WELL THEY SEE

QUALITY OF LIFE
  • WHAT IS IT?
    ▪ DIFFICULT TO DEFINE AND EVEN HARDER TO MEASURE
      ▪ MASSOF RW AND RUBIN GS
    ▪ 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

GLAUCOMA PATIENTS
  • QUALITY OF LIFE MAY BE IMPACTED BY
    ▪ DIAGNOSIS
    ▪ FUNCTIONAL LOSS
    ▪ TREATMENT

GQL-15 STUDY RESULTS

PSYCHOLOGICAL IMPACT
  • THE DIAGNOSIS ALONE HAS RAMIFICATIONS
  • FEAR OF BLINDNESS
  • ANXIETY

QUALITY OF LIFE PEARLS

CONCLUSIONS