GLAUCOMA: YOU MAKE THE CALL
Lori Vollmer, OD
Jessica Steen, OD
Greg Caldwell, OD
Joseph Sowka, OD

Please text us your questions!

Joe: 954-298-0970  Greg: 814-931-2030

PACHYMETRY
- Correct IOP or not?
- OCT vs Ultrasound?

WHAT IS MORE IMPORTANT?
TARGET IOP OR PEAK IOP?

TARGET IOP
- A clinical GPS
- How do you get there if you don’t know where you are going?
- Is it important? Yes
- How do I figure it out? That’s not so easy
- To get where you’re going, don’t forget where you have been.
  - Peak IOP
- Should we do it? Do we do it?

TARGET IOP
- Practice guidelines recommend target IOP
  - Should be written in chart
  - Rarely done so
- Determining initial target pressure
  - Existing disc damage
  - Extent of field damage
  - Risk of imminent/ future functional disability
    - Rate of change impacts target IOP
  - Patient age and life expectancy
  - Peak IOP
- “B” should have lower target IOP than “A”
SETTING A TARGET PRESSURE

Two Methods

- **Absolute Value**
  - Risk of over-treating or under-treating patients
  - What pressure is ideal for everyone?
  - One size fits all... doesn’t

- **Percentage decrease from baseline**
  - What constitutes an acceptable decrease?

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PERCENTAGE DECREASE FROM BASELINE

- Can the studies guide us?
- Clinical trials provide Evidence and Guidelines
  - Take care to apply the correct study to the correct population
- Understand how and why target pressures are chosen for clinical studies

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INFORMATION FROM MAJOR STUDIES

<table>
<thead>
<tr>
<th>Study</th>
<th>IOP reduction</th>
<th>Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>OHTS</td>
<td>20%</td>
<td>Yes</td>
</tr>
<tr>
<td>EMGT</td>
<td>25%</td>
<td>Yes</td>
</tr>
<tr>
<td>CNTGS</td>
<td>30%</td>
<td>Yes</td>
</tr>
<tr>
<td>CIGTS (med)</td>
<td>35%</td>
<td>No</td>
</tr>
<tr>
<td>CIGTS (Surg)</td>
<td>48%</td>
<td>No</td>
</tr>
<tr>
<td>AGIS</td>
<td>&lt; 18 all visits</td>
<td>No</td>
</tr>
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AGIS 7: SUSTAINED IOP BELOW 18 MM HG: POSITIVE CORRELATION WITH STABILITY OF VISUAL FIELD

- A target pressure is that pressure at which the sum of the impact of the glaucomatous vision loss upon the patient and the impact of treatment upon the patient is minimized.
- Once treatment is started, the goal is not to make the IOP ‘normal’, but safe for the patient.
- Demand greater reductions than before
  - 40-50% vs 20-30%, especially for advanced disease/risk of visual disability.
- Am I at medicolegal risk if I don’t have target in chart? No
- Am I at medicolegal risk if I have target in chart and I don’t reach it? No

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Are we setting target pressures too high?
WHICH IS BETTER? ONE OR TWO?
- Pt 1: treated 20 mm
- Pt 2: treated 15 mm

WHICH IS BETTER? ONE OR TWO?
- Pt 1: Ta max 42 mm - treated 20 mm
- Pt 2: Ta max 20 mm - treated 15 mm

TARGET IOP: A BEST GUESS BASED UPON:
- Age and longevity
  - Don’t be age-prejudiced
- Degree of optic nerve damage
- Degree of visual field loss
- Threat to fixation and risk of disability
- IOP at which damage occurred
- Corneal thickness
- Family history of glaucoma blindness

REASSESSING ‘TARGET’ IOP
- 72 YOBF: POAG OU x 6 years
- Initial IOP 28 mm
- Treated IOP: 15 mm
  - Can tolerate only 1 PGA as MMT
  - Adverse reactions with all other meds
  - Still an acceptable response, right?
  - 54% reduction

REASSESSING ‘TARGET’ IOP
- 68 YOF- OHTN
  - Marked late onset rapid progression in disc and field OD
  - OS stable throughout
  - Needs lower IOP
  - S/P SLT with PGA - IOP 11 mm Hg OU
**REASSESSING ‘TARGET’ IOP**

- Treatment advocated - pt declines; agrees to close observation
- 3 mos f/u scheduled - returns 3 years later

**CONCLUSIONS**

- Don’t over-treat those at minimal risk of vision loss
- Don’t under-treat those at high risk of vision loss
- Don’t focus on the IOP to the exclusion of other factors
- Remember to treat the patient, not a number

**WHAT ABOUT THE NEW STUFF?**

- Vyzulta
- Rhopressa
- iStent updates
- Cypass
- Xen Gel Implants

**VYZULTA™ (latanoprostene bunod ophthalmic solution, 0.024%)**

- First prostaglandin analog with one of its metabolites being nitric oxide (NO)
- QD dosing
- Dual mechanism of action
  - metabolizes into two moieties, latanoprost acid, which primarily works within the uveoscleral pathway to increase aqueous humor outflow, and butanediol mononitrate, which releases NO to increase outflow through the trabecular meshwork and Schlemm’s canal.
Netarsudil ophthalmic solution 0.02% (ROCK-NET Inhibitor) Triple-Action


3 Identified IOP-Lowering Mechanisms

- ROCK inhibition relaxes TM, increases outflow
- NET inhibition reduces fluid production
- ROCK inhibition lowers Episcleral Venous Pressure (EVP)

Netarsudil ophthalmic solution 0.02: Rocket 2 study

- Rocket 2 is a 12-month Phase 3 study of Netarsudil vs. Timolol
- The patient group to be used for Rocket 2 primary endpoint analysis was changed with FDA agreement
  - Primary endpoint analysis will include only patients with a baseline IOP above 20 mmHg and below 25 mmHg
  - Rhopressa QD and BID met criteria for non-inferiority to timolol (baseline < 25 mm)
- Seems to work best at lower/modest IOP baseline

Netarsudil ophthalmic solution 0.02%
Rhopressa

- In two phase III studies, more than half of patients experienced conjunctival hyperemia compared to 8% to 10% of timolol patients.
  - More complaints of eye redness with Rhopressa.
- 9% and 5% of Rhopressa once-daily patients reported corneal deposits across the two phase III studies compared to 0.4% and 0% of the timolol patients.
- Blurry vision was reported by 7% and 5% of Rhopressa patients compared to 3% and 0.5% of timolol patients in the studies.

ISTENT
(GLAUKOS CORP.)
iStent: Trabecular Micro-Bypass Stent
- FDA Approved 2012 for:
  - Mild to Moderate glaucoma in patients who need cataract surgery
  - No Bleb is formed
  - Few complications
  - Relatively Easy to perform

ISTENT ADVANCEMENTS

- iStent inject
  - Preloaded needle that injects two stents, for which Glaukos has completed a phase 1 clinical trial.
    - Involving patients unresponsive to two glaucoma medications, patients were randomized to receive one, two or three stents
    - Each additional stent gives an incremental decrease in intraocular pressure.

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**ISTENT ADVANCEMENTS**

- **iStent Supra**
  - Meant to treat patients with severe glaucoma
  - Suprachoroidal space
  - More collateral damage, bleeding and hypotony.

**CYPASS**

Supraciliary microstent that increases uveoscleral outflow.

It is implanted through a clear corneal incision and can be combined with cataract surgery.

**KAHOOK DUAL BLADE**

- Single use, ophthalmic blade
- Utilizes ab interno approach through a clear cornea micro incision
- Precision engineered to fit in the canal of Schlemm
- Dual blades positioned for precise parallel incisions of the trabecular meshwork with minimal residual leaflets
- Maintains natural physiologic outflow pathways

**KAHOOK DUAL BLADE**

- Tip of the blade is pierced across the trabecular meshwork, then the dual blades create two incisions as the blade is advanced.
- Beveling allows for apposition with outer wall of Schlemm’s canal and advancement of the dual blade neatly excises a strip of trabecular meshwork for 90 to 150 degrees of the angle.
- An analysis of post-op outcomes at three months found a 33% reduction in IOP, from 17.5 mm Hg pre-op to 11.8 mm Hg post-op. Sixty-nine percent of patients were able to stop using at least one of their glaucoma medications after surgery.
- Must have good visualization of the angle
- Vision can be decreased due to hyphema
- Can be used stand alone or with cataract surgery
FDA approved the XEN45 Gel Stent and the XEN Injector for patients with refractory glaucoma who failed previous surgical treatment or in patients with primary open angle glaucoma, pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.

- “Lower maintenance” bleb-forming procedure
- Potential for low (<15 mm) IOP

XEN GEL STENT

- The stent is a soft, permanent, subconjunctival implant that shunts fluid from the anterior chamber to the subconjunctival space.
- 6-mm long and the width of a human hair
- Preloaded in a disposable Xen injector and is implanted through a small, self-sealing corneal incision.
- The stent’s collagen-derived non-inflammatory gelatin material allows it to conform to the ocular tissue, possibly minimizing many of the issues seen with synthetic materials such as migration, erosion and corneal endothelial damage.

WHAT DO YOU DO WHEN YOU SEE A DISC HEMORRHAGE?

Joe: 954-298-0970; Greg 814-931-2030
Not all hemorrhages of the disc are disc hemorrhages. Make sure that the glaucomatous characteristics are there.

**RISK FACTORS: DISC HEMORRHAGES**

Inferior, inferior temporal, superior, and superior temporal regions of the disc are most susceptible and account for virtually all true glaucomatous disc hemorrhages. Typically occurs where notches and RNFL defects occur. Hemorrhages at other areas of the disc (nasal and temporal) tend to not be associated with glaucoma.

**OTHER CAUSES OF ‘DISC’ HEMORRHAGES**

- PVD
- HTN
- Anemia
- Diabetes
- Vascular occlusion
- Subarachnoid bleed
  - Terson’s syndrome
    - Subretinal and intraretinal
    - May be juxtapapillary

**ARE DISC HEMORRHAGES A RISK FACTOR FOR PROGRESSION OR ACTUAL PROGRESSION?**

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**EARLY MANIFEST GLAUCOMA TRIAL**

- Disc hemorrhages - predictive of progression
- Treatment was unrelated to the presence or frequency of disc hemorrhages.
  - Disc hemorrhages were equally common in both the treated and untreated groups of patients.
  - Disc hemorrhages don’t occur in all glaucoma pts.
- Disc hemorrhages cannot be considered an indication of insufficient IOP-lowering treatment,
  - Glaucoma progression in eyes with disc hemorrhages cannot be totally halted by IOP reduction.

**OCULAR HYPERTENSION TREATMENT STUDY**

- The occurrence of a disc hemorrhage increased the risk of developing POAG 6-fold in a univariate analysis and 3.7-fold in a multivariate analysis that included baseline factors predictive of POAG
- Occurrence of an optic disc hemorrhage was associated with an increased risk of developing a POAG end point in participants in the OHTS
  - However, most eyes (86.7%) in which a disc hemorrhage developed have not experienced a POAG end point to date

**55 YOM**

- 2012 presents without complaints
- BCVA 6/6 OD, OS
- IOP:
  - OD: 27 mm; 30 mm
  - OS: 15mm; 15 mm
- CCT: 536; 531

**55 YOM**

- Treatment initiated
  - IOP drops to mid teens OU
- Optic disc change OS noted 4/14
- Therapy amplified
  - 7/15: latanoprost and dorzolamide/timolol FC OU
- IOP: 10 mm OU
- CCT: 536; 531
SO WHAT DO I DO WHEN I SEE A DISC HEMORRHAGE?

- **(Treated) IOP high teens:**
  - Progression documented - increase therapy
  - Risk of visual disability - increase therapy
  - None of the above: increase therapy or monitor for progression then increase therapy

- **(Treated) IOP low teens**
  - Monitor for progression (if safe) - no change
  - Progression documented or risk visual disability
    - Therapy increase
    - Equal risk of blindness from disease or treatment

HOW DO YOU MANAGE GLAUCOMA SUSPECTS?

- Elevated IOP/ OHTN
- Suspicious disc appearance
  - Thin rim tissue; Disc asymmetry
- Suspicious RNFL/ OCT
- Disc hemorrhage
- Suspicious visual field loss
- Family history of glaucoma
- Age
- Race
- Phakic hyperopia- angle closure suspect

DISC EVALUATION

- Size
- Rim color
- Focal rim defects (notching)
- Hemorrhages
- RNFL defects
- Parapapillary atrophy
WHICH OF THESE 3 PATIENTS DO YOU MOST SUSPECT HAS GLAUCOMA?

PATIENT 1: 28 YOF

- IOP: 11 mm
- CCT: 610

PATIENT 2: 56 YOM

- IOP: 22 mm
- CCT: 598

PATIENT 3: 64 YOF

- IOP: 31 mm
- CCT: 490

WHICH PATIENT HAS GLAUCOMA? 1? 2? 3?

- IOP: 11 mm
- CCT: 610

- IOP: 22 mm
- CCT: 598

- IOP: 31 mm
- CCT: 490
RULE: WHEN DIAGNOSING GLAUCOMA, TAKE IOP OUT OF THE EQUATION

(When managing glaucoma, put IOP back into the equation...but that’s another lecture.)

WHO ARE THE GLAUCOMA SUSPECTS?
- Large cupping - normal IOP
- Large cupping - high IOP
- Normal cupping - high IOP

IS THIS GLAUCOMA?
34 YOHF
“Highly suspicious” ONH OU
IOP statistically normal
- 13 mm Hg OU
Average CCT
Previously treated for NTG

IS THIS GLAUCOMA?
78 YOWM
Annual exams with multiple doctors
IOP ranges from 17 – 21 mm Hg
CCT 570
Ocular health always “normal”
Small discs with indistinguishable cupping
- 0.2/0.2 – 0.3/0.3

My advice to patients: If you insist on having a suspicious optic disc, you had better be a good field taker.
DON’T OVER-TEST

“When you get the answer you want, hang up”

Joe: 954-298-0970; Greg 814-331-2030

BUT DON’T UNDER-TEST, EITHER

WHO ARE THE GLAUCOMA SUSPECTS AND WHAT DO I DO?

- **Large cupping - normal IOP**
  - Does the nerve look glaucomatous?
    - Yes - photos, fields, pachymetry, gonio, OCT
    - No - OCT - if normal-done, if abnormal - fields - if normal - done, if abnormal - monitor
  - **Large cupping - high IOP**
    - Does the nerve look glaucomatous?
      - Yes - photos, fields, pachymetry, gonio, OCT
      - No - OCT, photos, pachymetry, fields, gonio
  - **Normal cupping - high IOP**
    - OCT, photos, pachymetry, fields, gonio

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LARGE CUPPING - NORMAL IOP

Annual exams
LARGE CUPPING- UNKNOWN IOP-
DIAGNOSED WITH GLAUCOMA

- 46 YOF
- Diagnosed and treated for glaucoma in Jamaica
- Brimonidine 0.1%; latanoprost/timolol FC OU
- IOP: 14 mm OD, 16 mm OS
- CCT: 530; 528
- 0.75/0.75 OU
- Fields unreliable- high FP

Joe: 954-298-0970; Greg 814-831-2030

LARGE CUPPING-
HIGH IOP

56 YOF
IOP: 24 mm OH
CCT: 550 OD, 539 OS
RTC 6 mos fields
Follow w/o treatment Q 6 mos

.NORMAL CUPPING-
HIGH IOP

IOP: 30 mm OD, 32 mm OS
Mother + glaucoma (10-2 field)
Rx: Latanoprost OU

56 YOM: mother had glaucoma
CCT: 548 OU
Peak IOP: 29 mm

Make a decision! Patients shouldn’t be ‘glaucoma suspects’ for ten years. Either they have the disease or they don’t.

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