What’s New, What’s Next in Glaucoma
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Disclosures
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What’s New, What’s Next

• Can a biomarker be developed to diagnose glaucoma?
• How often does glaucoma occur?
• IOP
  • 24-Hour IOP
    • Devices now FDA approved to measure 24-hour IOP
  • Ocular Perfusion Pressure
    • Including blood pressure in equation to measure blood flow to optic nerve
  • Role of biomechanics and glaucoma risk
    • Hypertension
    • Gonioscopy
  • Cerebrospinal fluid pressure and translamellar pressure difference
    • One explanation for why glaucoma may develop at low IOP

What’s New, What’s Next

• Optic Nerve/RNFL/Posterior pole
  • What changes first – RNFL or optic nerve or macula?
    • Important to get measurements from all areas to better understand and diagnose disease
  • Visual fields
    • Role of central fields in diagnosing and monitoring glaucoma
      • 10-2 pattern with 2° spacing
      • Faster tests
        • SITA Faster
  • OCT
    • Role of OCT angiography
      • Modifying how the OCT RNFL results are displayed
        • Improving the TSNIT that allows easier detection subtle thinning and improved structure-function
  • Artificial intelligence
    • Deep learning

What’s New, What’s Next

• Therapy
  • Generics
    • >70% of glaucoma prescriptions
  • Do glaucoma medications work around the clock?
    • FDA does not require 24 hour testing
  • New medications
    • Vyzulta, Rhoressa
  • New drug delivery devices
    • Ring, Betoptic SR, plugs
  • Fixed combination agents have moved up to 2nd line agents
  • New glaucoma surgical devices such as Xen implant, Cypass, iStent
  • MIGS type devices with new ones coming quickly
  • Artificial intelligence
    • Deep learning
Artificial Intelligence (AI)  
Deep or Machine Learning  

What’s New, What’s Next  
Restoring Vision: Retinal Cell Regeneration  
• Encourage nerve fiber growth by removing inhibitory factors  
• Nanotechnology  
  • Protein nanofiber structure to allow fibers to grow  
• Cellular implants  
  • Engineered cells that provide cellular support and regeneration  
• Genetic recognition and manipulation  
• Promoters of nerve growth  
• Stem cell  
  • Multipotent stem cells are retrieved from tissues such as bone marrow

Is there anything new about angle closure glaucoma?  
How does one treat acute angle closure glaucoma?  
Has the treatment changed?

How Often Does Glaucoma Occur?  
Much greater than previously thought
IOP and Blood Pressure

- Central Corneal Thickness
- Does it change with age?
- 24-Hour IOP
- Ocular perfusion pressure
  - Diastolic blood pressure minus IOP
  - Cut off is b/w 30 and 50
- Role of hysteresis in glaucoma risk
- CSF and glaucoma risk

How does the new guidelines to aggressively lower BP impact glaucoma care?

Nocturnal Systemic Hypotension Increases the Risk of Glaucoma Progression

How Does the IOP Vary During a Day?

24-Hour IOP Monitoring

- How do we evaluate IOP if we are only measuring it briefly in office?
- Three approaches to measure IOP over 24 hour period
  - Self tonometry
  - Permanent continuous IOP monitoring
  - Temporary continuous IOP monitoring
Permanent Continuous Monitoring

- Provide daytime and nighttime IOP measurements through self-contained implant
- Accessed remotely with wireless technology
- Ideal for advanced glaucoma
- Would not be measuring the surface but rather taking IOP measurements directly inside the eye
  - Subject to less noise
- Incorporates telemetric IOP device with IOL
- Digital signal sent form IOL to external device
- Alarm raised at certain point
- Long-term stability is unknown

Self Tonometry

- Patients would monitor their IOP over time with easy-to-use devices
- Easiest approach in regards to continuous monitoring
- Adapt current device such as Noncontact tonometer or Rebound tonometer
- May be difficult for some patients to perform
- Not easy to obtain 24 hour IOP

Cerebrospinal Fluid Pressure (CSF) and Glaucoma

- Recent work has shown that low CSF may be contributory to the development of glaucoma
  - Translaminar pressure differential
    - Takes into account the IOP and CSF
    - May explain pathogenesis for normal tension glaucoma

Equinox Googles

- Method to equalize translaminar pressure by changing pressure in front of eye – Atmospheric pressure
- Translaminar pressure differential between IOP and CSF
- Googles in development
- Patient would wear them during night, similar to CPAP device
- Question of how long googles need to be worn and treatment effect still in investigation
Central Visual Fields and Glaucoma

- Recent papers have suggested that the 24-2 test pattern has limited ability to detect central field defects
  - 60% of retinal ganglion cells are found within 4.5mm of fovea
  - Macula region comprises only 10% of overall visual field area though it is responsible for 60% of area of visual cortex
  - Damage to central 10° associated with diminished contrast sensitivity, reduced reading ability

Glaucoma Pearls

- Therapy
  - Do Medications work around the clock
  - Fixed combination agents in glaucoma
  - New glaucoma surgeries
  - New Medications
  - Drug delivery devices

What’s New, What’s Next

Therapy

- There are 6 classes of IOP-lowering medications
  - Each works by altering 1 or more aspects of aqueous humor flow
  - Beta-blockers and carbonic anhydrase inhibitors reduce the rate of aqueous production
  - Prostaglandins increase outflow through the uveoscleral pathway
  - Alpha-adrenergic agonists lower IOP by a dual mechanism
    - reducing aqueous production and increasing uveoscleral outflow
  - Miotic class of drugs do increase trabecular outflow, but only indirectly through actions on the ciliary muscle
    - not through any direct effects on the TM itself
    - generally poorly tolerated and not widely used in modern practice
  - Rhopressa (ROCK inhibitor) and Vyzulta (PG + Nitric Oxide) work at the TM
    - the main site of outflow obstruction in glaucomatous eyes

New Drugs

- Vyzulta– Latanoprost bunod - Nicox
  - Nitric oxide donating Prostaglandin F2α
  - Bausch & Lomb – Approved Nov 2018
  - Uveoscleral and TM outflow
- Rho Kinase Inhibitors –Netarsudil 0.02%
  - Rhopressa and Roclatan
  - With and Without Latanoprost
  - Aerie – Approved December 2018
  - Enhance TM outflow

Latanoprostone bunod (Vyzulta)

- Novel nitric oxide-donating prostaglandin F2-alpha analog
- 0.024% used once daily to reduced IOP
  - Bausch & Lomb
- Metabolized to latanoprost acid plus butanediol mononitrate
- Butanediol mononitrate is a nitric-oxide donating moiety that can dilate blood vessels and also reduce IOP
- Works over 24 hour period with >35% IOP reduction
- Uveoscleral and Trabecular Meshwork outflow

New Medication

Rho Kinase Inhibitors

- Rho kinase inhibitors
  - Rhopressa
  - Reduce cellular stiffness in trabecular meshwork
    - Target trabecular meshwork cells to enhance outflow
  - May offer neuroprotective as well as anti-inflammatory effects
  - Aerie
- Side effects
  - Hyperemia
  - Conjunctival hemorrhages
  - Corneal verticillata
  - Efficacy similar to timolol
  - Once per day
**Roclatan**
- Combination of Rhopressa with latanoprost
- Dosed once daily with significant IOP lowering
- Few systemic side effects
- Limited ocular side effects
- Expected 1st quarter 2019

**Drug Delivery**
- Ensure drug delivered to the site of action in the eye
- Reduce side effects of topical medications
- Improve compliance
- Improve clinical outcomes

**Drug-Loaded Contact Lenses**

**Drug Loading Strategies**
- If CL is to contain medication, this combination must be as safe and effective as CL and drug is used singly
  - Cannot impact upon refractive properties of eye
  - Concern for preservatives concentrating in CL or concentrating in tear layer between CL and cornea
- Use colloidal nanoparticles or molecular imprinting
  - Sub-micron size particles either coated with or encapsulating drug
    - Liposomes
    - Colloidal gold or silver
    - Once CL is placed on eye, drug diffuses into tear layer
  - Drug imprinting
    - Modifies contact lens material to allow drug molecule to sit within hydrogel complex
- Allowing higher drug load than simple diffusion

**Bimatoprost SR**
- Allergan
- Sustained release prostamid-loaded bioerodible implant that will last 4-6 months with similar efficacy to eyedrops
- Injected into the anterior chamber using Novadur injection system
- Can be performed in the office
- Ensures patient compliance

**Glaucoma Surgery**
- Minimally Invasive Glaucoma Surgery (MIGS)
  - Objective is reduced complications compared to trabeculectomy with nearly similar IOP reduction
  - Position of device
    - TM, Suprachoroidal space, Subconjunctival
  - New MIGS type devices in development
    - To be approved over the next several years
    - IStent inject and IStent Supra (Glaukos), iVantis (Hydrus), CyPass Micro-stent (Tracend Medical), Aquelix (Allergan)

**Summary**
- Many developments in terms of new diagnostic devices
  - IOP measuring
  - OCT imaging
  - Visual Fields
- And therapeutic entities
  - Medications
  - Surgical advances