A Roadmap for the Medical Management of Glaucoma

Ben Gaddie, OD, FAAO
Eric Schmidt, OD, FAAO

1

Disclosure Slide for Dr Eric Schmidt

- Dr Schmidt is an advisor or consultant for the following:
  - Allergan
  - Tarsus
  - Eyenovia
  - Trukera
  - Thea Pharmaceuticals
  - Topcon
  - BBL
  - Sight Science
  - Avellino Labs
  - Ynsus
  - Sydnexis
  - Harrow Pharmaceuticals

2

To Treat or Not To Treat, That Is The Question!

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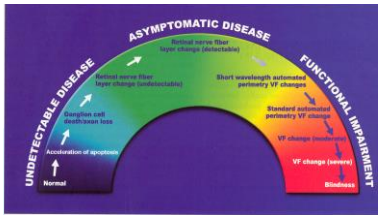

4

A Review Of Risk Factors

- FINDACAR
  - Family history
  - IOP
  - Nearsightedness
  - Diabetes/Vascular disease
  - Age
  - Corneal thickness
  - Asymmetry
  - Race

5

Glaucoma Risk Factors

- FINDACAR
- The more risk factors one has, the more likely one is to develop glaucoma
- The more risk factors one has, the lower the IOP target should be

6

How Can We Make A Difficult Decision Less Difficult?

- Get Data
- What Data?
  - OCT
  - VF
  - FP
  - IOP
  - IOP
  - Pachymetry
  - Fam Hx
  - IOP

7

- Glaucoma suspects can be (broadly) categorized into two groups:
  1. Ocular hypertensive subjects with risk factors for the future development of glaucoma
     - **These patients are addressed by OHTS data and who to treat**
  2. Subjects with questionable glaucomatous findings that cannot definitely be distinguished from normal
     - e.g., suspicious appearance of optic disk, RNFL/GCA or VF and IOP that is 21 mmHg or lower

8

Open Angle Glaucoma Suspect

- **The Decision Tree:**
  - The patient **without** OCT, VF or ONH damage
  - This may be someone with IOP <21 or <21 mmHg

9

- Rather than a simplistic approach of treating everyone with an IOP of over 21 mmHg, treatment is held off until there is sufficient evidence of glaucoma damage at some level (OCT, VF,)
  - This is a practice philosophy that can be followed for *low risk* patients
- Or, we elect to treat those with the most significant risk factors.

10

- *IOP 21-30+ mmHg with*
  - Normal appearing or suspicious optic nerve, But NO definitive changes!
    - no visual field defects
  - some risk factors
- Follow OHTS Treatment Guidelines:

11

- Management Options:
  - no single treatment plan nor guidelines, varies with every patient, must be individualized
1. Follow these patients every 3-6 months with observation and repeated: OHN, VF, OCT, IOP
   - Wait until confirmation of true OCT/VF defect, OHN change
2. Or, may initiate therapy for those with 3 or more risk factors: positive family history,
   - C/D ratio 0.8 or greater, asymmetry of the nerve heads
   - African-American; diabetes, etc.
   - Questionable visual field defects, fluctuating IOP

12

- At any IOP
1. Glaucomatous OHN Changes
   - As identified by you or via photograph, OR
2. Strongly abnormal, characteristic and reliable OCT
   - This must have some "clinical correlation"
   - Rarely do you treat based upon this alone (patient has other findings)
   - Watch out for "Red Disease"
3. Characteristic/Confirmed Visual Field Loss

   (*not required for diagnosis*)
- OHTN with IOP over 30 mmHg
  - Some exceptions; eg very, thick cornea

13

Glaucoma diagnosis can be a very complex

- Requirements
  - Organized, step-by-step approach
  - Sort and organize the data
  - Identify good data
  - Ignore bad/unreliable data
  - Confirm data when necessary
  - Sort and organize again
  - No need to rush your decision
  - Individualize to your patient
- Begin therapy (later) or monitor

14

When you have enough compelling evidence -you treat!

- Look to the OHTS Study for guidance
- Look to Murray for guidance!

15

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Ocular Hypertension

When do you treat – sometime, all the never, never?
Can OH progress to glaucoma if it is treated?
What are the downsides to therapy?
When not treat everyone w elevated IOP?

16

Ocular Hypertension

- Definition of ocular hypertension
  - IOP 21 mm Hg or higher
    - Based upon Armaly statistical definition of OHTN
    - Not based upon clinical findings
  - Visual Fields Full
  - Optic nerve considered Full
    - This part of definition is changing with OCT use allowing subtle optic nerve/RNFL changes to be detected
- Consider therapy based upon risk of developing glaucoma over lifetime
  - Concept of risk assessment
- Therapy is often considered optional since true damage is not present
- Still not clear if early therapy (before damage) alters long-term outcome
  - OHTS III was meant to answer this question

17

The Swinging Pendulum of Therapy for Ocular Hypertension

- 1960s IOP > 21 mm Hg Treat
- 1970s IOP > 21 mm Hg No Tx
  - Decade of Ocular Hypertension
- 1980s IOP > 21 mm Hg Tx/No Tx
  - 1982 Quigley paper field loss late sign OAG
  - Concept of risk factor analysis
- 1990s IOP > 21 mm Hg Tx/No Tx
  - Earlier therapy once latanoprost introduced

18

Ocular Hypertension

- Many years ago, everyone with elevated IOP was treated
- Recognition that about 1% per year convert from OHTN to glaucoma
- Those converting have greatest risk
  - thinner cornea, African American, larger cupping
- Led to the concept of risk assessment
- OHTS provided information on when to treat
  - European Glaucoma Prevention Study (EGPS) also provided risk information

19

20

Treating ocular hypertension
Risk assessment

- Consider number of risks individual has that increases chance for
  - Conversion of ocular hypertension to the development of glaucomatous damage
  - Based upon evidence
- Studies include Ocular Hypertension Treatment Study (OHTS) and European Glaucoma Prevention Study (EGPS)
- If we are going to treat ocular hypertension, at what risk level?
  - 10% vs. 15% vs. 20%
  - Begin prophylactic therapy
- Uses concept from Framingham Heart Study

21

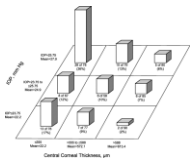
Risk Calculator in Glaucoma

- Whom and when to treat Ocular Hypertension (OHTN) is not well defined
  - OHTS study provides data on conversion rates
  - Use this data to determine when to treat
  - Still problem with OHTS study is that it was done primarily in Caucasian cohort
- Treatment of Hypertension and Elevated Cholesterol are similar to OHTN therapy
  - Coronary Heart Disease (CHD) and Glaucoma are chronic diseases w modifiable risk factors
  - Treatment outcomes differ between conditions
    - Glaucoma chronic
    - CHD can result in sudden death
  - Approach in developing prevention strategies is similar

22

Risk Assessment

- Risk Level Low < 5%
  - Monitor
- Risk Level Moderate 5-15%
  - Consider Therapy
  - Discuss with patient
- Risk Level High >15%
  - Treat



23

iPhone Risk Calculator

24

Risks

- OHTS
  - IOP
  - Corneal thickness
  - Cup/Disc ratio
  - VF status
- Other risks
  - Family history
  - Race including Hispanic
- Newer risks
  - Alcohol use
  - Cigarette smoking
  - Diabetes?
  - Age at menopause
  - Ovarian surgery
  - Physical activity
  - Metabolic diseases
    - Hypertension, cholesterol, Cardiopulmonary diseases
  - Sleep apnea

25

Ocular Hypertension

- Treat when risk is significant but….
- Need to include patient in discussion about therapy
- Some patients would like OHTN to be treated when risk is present while others would rather not be treated
- Glaucoma is a slow- moving disease so can monitor those with OHTN safely without therapy
- Still not clear how soon therapy should be initiated

26

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Starting Therapy

Target IOP

27

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Medical Options

28

29

Glaucoma Treatment Universe 2024

- Prostaglandins
- Alpha agonists
- Rho-kinase Inhibitors
- Beta-blockers
- Carbonic Anhydrase Inhibitors
- Combo Agents
- SLT
- MIGS
- Glaucoma Surgery
- How Do You Know Which Category To Choose???

30

What Are You Trying To Achieve?

- Optimal IOP Reduction
- Minimal Side Effects
- Rigid Compliance
- Anything Else?

31

Prostaglandin analogs

- Lower IOP by enhancing uveoscleral outflow
- They also reduce episcleral venous pressure
- PGAs work by causing up to a 26% reduction in resistance to outflow
- Breaks down collagen in the uveoscleral meshwork
- Create new channels for outflow

32

PGA

- QHS dosing
- Long duration of action
- Flatten diurnal curve
- Effective on trough and peak IOP
- No systemic side effects
- Little tachyphylaxis

33

Prostaglandin Side Effects

- Conjunctival hyperemia: Severe hyperemia
  - Lumigan 3.5%
  - Travatan 1.5%
  - Xalatan <1%
  - Vyzulta?? Iyaaahh?
- Is this a transient phenomenon?
- Is it an allergic conjunctivitis?
- Is it worth stopping the drop?

34

Conjunctival hyperemia

- PGAs have an effect on EP receptors which are vasodilators
- The stronger the drug binds to that receptor the more pronounced the vasodilation effect will be -
  Oh Really!!
- Will switching from 1 PGA to another decrease the hyperemia effect?

35

Prostaglandin Side Effects

- Iris pigmentation
  - Is it reversible?
  - Is it pre-cancerous?
- Xalatan - 6.7% @ 6mths
  16% @ 12mths
- Travatan - 3% @ 12 mths
- Lumigan - 1.9% @ 12mths
- SO?

36

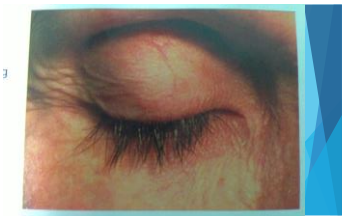
Other Prostaglandin side effects

- CME
- Uveitis
- Reactivation of HSK
- Hypertrichosis
- Periorbital skin darkening
- Periorbital fat atrophy

- One must take into consideration the benefits of low IOP with the risks of the side effects

37

37



38

Prostaglandins

- Oh sure, we know they are good, but just how good are they?
  - Average IOP drop of 34%
  - Improved compliance
  - Excellent safety profiles

- In general, PGAs are the initial therapy of choice.

39

39

Prostaglandins

- All decrease IOP by increasing uveoscleral outflow
- All are effective at squashing the diurnal curve
- They have either no effect or a positive effect on retinal perfusion
- Some affect nitric oxide at the optic disk
- Some have BAK, others don't
- But does 1 work better than the others?

40

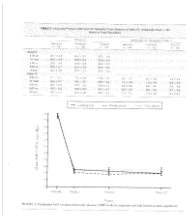
40

XLT Study – Parrish, Palmberg, et. al.
(AJO, May 2003, Vol. 135, No.5)

- Multicenter study to compare IOP lowering efficacy of Bimatoprost vs Latanoprost vs Travaprost
- Also compared safety profiles of the 3 drugs
- Conclusions: All 3 drugs were comparable in their ability to lower IOP at all time periods.
  - Latanoprost exhibited greater ocular tolerability

41

41



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- Reduces IOP by 32%
- 1.2mm HG lower than latanoprost
- Preserves VF better by 10%
- No loss of effect while sleeping

- Improved side effect profile

- Releases nitric oxide at the trabecular meshwork level

43

43

- Effect of latanoprostene bunod on Optic Nerve Head Flow
  - Samaha, Diaconu et al, IOVS, Feb 2022, Vol 9, Iss 2 pp172-176

- Purpose was to evaluate effect of latanoprostene bunod on optic nerve blood volume and O2 saturation - *IN HEALTHY SUBJECTS*

- Measurements were taken before initiating therapy and then 7 days after QD therapy of both Latanoprost and latanoprostene bunod

44

44

- ONH saturated O2 levels were 4% higher with Vyzulta than latanoprost

- ONH blood volume was way higher with Vyzulta
  - 66% higher at Hr 1, 45% higher at Hr 2

- What is the clinical significance of this?

45

45

Are generics really as good as branded products?

What about when it comes to prostaglandins?

46

46

But really… Is There Anything New??

Iyuzeh-
(latanoprost 0.005%)

Thea Pharmaceuticals

Let's talk about this…

47

- Does that sound familiar?
- Monoprost (in Europe) - the market leader in PGA in Europe
- This actually is PRESERVATIVE FREE latanoprost!!
- Single dose container
- But does it really work??

48

Iyuzeh - Phase 3 data

- Compared to Xalatan (Switch Study)
- Stable POAG pxs on Xalatan
- 8 day washout period
- 3 months on Iyuzeh
- IOP reduction was 4-8mm Hg on Xalatan
- IOP reduction was 3-8mm Hg on Iyuzeh
- Baseline IOP was 19mmHG!!

49

Iyuzeh - Phase 3 data-Adverse Effects

- Xalatan group
  - Hyperemia - 31%
  - Eye Irritation - 34%
- Iyuzeh Group
  - Hyperemia - 34%
  - Eye Irritation - 19%
- ZERO reports of SPK

50

- European data - Higher baseline IOP (24mm Hg)
  - IOP lowered to 15.5mm Hg
  - Same rate of adverse effects
- Bachnach data (2023 AGS)
  - 12 week trial comparing to Xalatan
  - Similar IOP reduction (as measured by ability to get IOP <18mm Hg)
  - 2% experienced redness or ocular irritation
  - 0% SPK

  Fewer ocular side effects (13.9% vs 22.5%)
- PAGSY study
  - 93% tolerated drop
  - 47 usage decreased 24%

51

#What's The Big Deal??

- OSD is an epidemic in glaucoma
- Will this improve compliance?
- Will this cost $1M??
- Is it better than what we have?

52

Are we going to see a trend towards Preservative free glaucoma drops??

53

Beta-blockers

- 40 year history of successfully lowering IOP
- Reduces aqueous humor formation
- Adrenergic agonists
- Lowers IOP 22-28%
- Ocularly well tolerated

54

Beta-blocker side effects

- Cardiac problems
  - Bradycardia
  - Hypotension
  - Exercise intolerance
  - Heart block
- Respiratory problems
  - Bronchospasm
  - Status asthmaticus

55

Beta-blocker side effects

- CNS
  - Often overlooked
  - ACID
    - Anxiety
    - Confusion
    - Impotence
    - Depression
  - General decreased affect
- Diabetic problems
  - Decreased sense of caloric need due to depressed adrenergic surge

56

Beta-blocker side effects

- 22% of pxs have contraindication to or significant side effect from beta-blocker
- Question, query and query some more!
- Be specific
- Remember the dose relationship so:
  - ½% rather than ½%
  - QD rather than BID
- They are real (may be anecdotal)

57

Works at the cellular level within the trabecular meshwork

ROCK inhibitors improve outflow by relaxing contraction and stress fibers at the t.m.

58

0.02%)

- Rhopressa QD is non-inferior to timolol 0.5% BID in lowering IOP
- Expected IOP reduction 3.7 -7.0mm Hg
- Rhopressa seems to better at lowering IOP (as compared to itself) in pressures < 25mm Hg
- IOP lowering effect is maintained over 12 months
- Was given a broad label by FDA

59

- Generally well tolerated
- Conjunctival hyperemia - 53%
  - Did not worsen with time
  - Mild-36.8%, moderate - 10.5%, severe -0.6%
  - D/C rate due to redness - -3%
- Corneal verticillata - 18%
- Conjunctival hemorrhage - 15%
  - All are transient and considered mild

60

- New MOA so… it is absolutely different
- It should be additive
- Definitely works better at lower IOP
- What about side effects?

61

M.O.S.T. Study

- Real World Open Label Phase 4 Study
- ASCRS 2020
- To determine efficacy of Rhopressa as an adjunct med
- Investigator's Choice – Rhopressa + any other agent
- 24.4% African-American participants

62

M.O.S.T. Results

Rhopressa + PGA - IOP 21.1> 16.9 mmHg (20% reduction)

Rhopressa + 2 meds – 20.6 > 16.6 mmHg (20% reduction)

Notice the low baseline IOP

63

More M.O.S.T. Results

- % of pxs less than < 18mm Hg
  - <18mm -72.7 % (from 34.4%)
  - <17mm- 65% (from 25.2%)
  - <15mm -40.6% (from 15.9%)
  - <14mm- 30.1% (from 11.3%)
- 2/3 of all patients achieved IOP < 17mm Hg

64

M.O.S.T. Tolerability rates

Hyperemia – 20.* %

D/C rate – hyperemia 3.4%

Tolerability rating

67.8-73.1% good or decent (physician response)

65-78% good or decent (Patient response)

65

Roclatan – Aerie

- Fixed Combination drug – Rhopressa + latanoprost
- QD dosing
- "Quadruple acting" MOA – (adds increased uveoscleral outflow)
- IOP lowering better than either of its components
- Potential to be very effective – lowered IOP an additional 2-3 mm compared to Rhopressa (and other PGAs)

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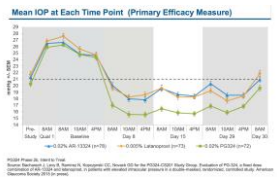

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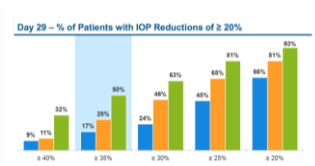

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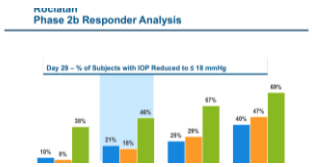

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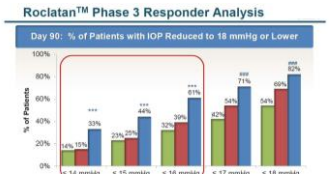

70

Newest Rocklatan Data

1400 pxs

Rocklatan vs Rhopressa vs Latanoprost

71

Newest side effect data

- No tachyphylaxis at 12 months
- No unexpected A.E.
- Very few serious A.E.- majority are mild

- 58% hyperemia but 5% d/c rate
- 20% Instillation pain – 0% d/c
- 10% subconj heme – 0% d/c

72

Adrenergic Agonists

- Dual mechanism of action
  1. Reduce aqueous production
  2. Enhance outflow mechanisms
- 22-28% IOP reduction
- Short duration of action
- TID dosage
- Avoid in kids

73

73

Mechanism of Action of Brimonidine-PURITE®

- Complements PGAs because it decreases aqueous production
- Complements timolol because it increases uveoscleral outflow

74

74

Brimonidine side effects

- 10-20%
  - Hyperemia
  - Allergic conjunctivitis
  - Ocular pruritis
- 5-9%
  - burning sensation,
  - conjunctival folliculosis,
  - ocular allergic reaction,
  - oral dryness,
  - visual disturbance
- Do these worsen with time?
- How do you know if the drops are the culprit?

75

75

Alphagan systemic side effects

- Dry mouth (~20%)
- Fatigue (1-2%)
- Drowsiness
- Decreased BP
- This drug can cross blood-brain barrier, esp in older and younger pxs

76

76

Brimonidine questions

- What is the correct dosage?
- Which of the 3 products should be prescribed?
- Can it be used as stand alone therapy?
- Effect on diurnal curve?
- What Happens If Hypersensitivity To 0.2% Brimonidine Occurs?

77

77

Let's talk (quickly) about combo drops!

- What are their advantages?
- What about their side effects?
- Are they twice as good as their individual components?

78

78

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Drug Delivery Options

Is this where therapy is going?

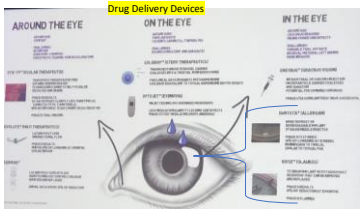
79

80

Drug Delivery

- Why
  - Reduce need for patient to take their drops
  - Host of studies have shown majority of eydrops not taken
    - Leads to worsening of condition
- Different ways to get medication into eye
  - Inject into AC
  - Contact lens
  - Punctal plug
  - Mist spray/thicken drug increasing contact time
  - Reservoir tacked into trabeculum
- Types – temporary vs. semi-permanent vs. permanent
- What are the downsides?
  - Cost? Does procedure and implant outweigh cost of eyedrop?
  - Side effects of medication
  - Complications for placing medication into eye

81



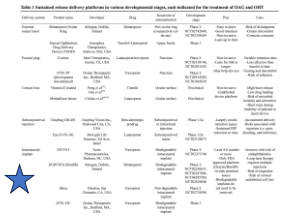
82

Drug Eluting Ocular Implants

- Unmet needs; Compliance, Compliance, Compliance!
  - forgetfulness, physical or cognitive disability
  - cost
  - side effects
- Locations;
  - Subconjunctiva, Lacrimal puncta
    - higher concentration, must cross ocular barrier; cornea, sclera
    - periocular side effects may be similar to topical application
  - Intraocular
    - lower quantity of drug required, higher concentration
    - at target tissues, fewer barriers, fewer periocular side effects
- Challenges – biocompatible device, sufficient drug content, constant drug release, ease of implantation

Seal JR, Robinson MR, Burke J, Bejanian M, Coote M, Attar M. J Ocul Pharmacol Ther. 2019;35:50–57.

83



84

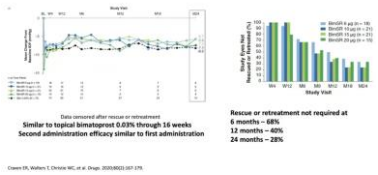
Bimatoprost SR (Durysta)

- Allergan
- Sustained release bio erodible implant that lasts 4-6 months with similar efficacy to eyedrops
- Small dissolvable pellet is injected into the anterior chamber
  - Sits in/near the angle that resorbs over time
- Can be performed in the office
- Insert can be visualized in the inferior angle
- Ensures patient compliance

85

86

BIM SR (Durysta) Phase I/II Apollo Trial: Efficacy



Data censored after rescue or retreatment

Similar to topical bimatoprost 0.03% through 16 weeks
Second administration efficacy similar to first administration

Rescue or retreatment not required at
6 months – 68%
12 months – 40%
24 months – 28%

Craven ER, Walters T, Christie WC, et al. Drugs. 2020;80(2):167-179.

87

Glaukos Announces Positive Results for iDose TR Exchange Trial, Highlighting Favorable Safety and Tolerability

January 10, 2023 04:05 PM Eastern Standard Time

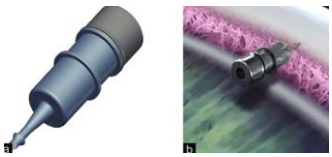
ALISO VIEJO, Calif.--(BUSINESS WIRE)--Glaukos Corporation (NYSE: GKOS), an ophthalmic medical technology and pharmaceutical company focused on novel therapies for the treatment of glaucoma, corneal disorders and retinal diseases, today announced positive results for a prospective, multi-center clinical trial designed to evaluate the safety of the surgical exchange procedure for iDose® TR (travoprost intraocular implant) in subjects who had previously been administered an iDose TR in the Phase 2b clinical trial (referred to as the "exchange trial").

"We are pleased to clinically confirm the iDose TR exchange procedure is safe and facile. We look forward to including these positive data in our upcoming NDA submission to further support the safety and tolerability of reloading iDose TR patients over time"

Tweet this

Results from the exchange trial demonstrated a second administration of iDose TR and removal of the original iDose TR implant was safe and well-tolerated, with the second iDose TR demonstrating a favorable safety profile over a 12-month evaluation period. Additionally, no subject in the exchange trial exhibited a greater than 30% endothelial cell loss over the extended evaluation period of more than five years on average. Glaukos plans to include the exchange trial's positive data set in its upcoming U.S. Food and Drug Administration (FDA) New Drug Application (NDA) submission targeted for the first quarter of 2023.

88



89

What's new in the glaucoma world?
Glaukos Corporation has released positive results from a prospective, multi-center clinical trial assessing the safety of the iDose TR (travoprost intraocular implant) surgical exchange procedure in patients who were administered an iDose TR in a previous phase 2b clinical.

Tell me about the iDose TR.
The iDose TR is a biocompatible titanium implant administered during micro-invasive procedures that contains a novel formulation of travoprost – a prostaglandin analog used to lower IOP—which is released inside the anterior chamber.

By eluting the drug already inside the eye, the device can then bypass the corneal permeability barrier, enabling the release of micro-amounts of travoprost over time.

How long does the implant last?
Glaukos designed the iDose TR to continuously release therapeutic medication levels for at least 1 year. Once all the travoprost is released, the implant is removed and replaced with another implant.

What was the purpose of this trial?
The exchange trial was based on an FDA agreement and was created to assess the safety and feasibility of exchanging iDose TR implants in patients who had received an iDose TR in a previous trial.

90

March 2, 2022

Johnson & Johnson Vision Care Receives FDA Approval for ACUVUE® Theravision™ with Ketotifen – World's First and Only Drug-Eluting Contact Lens

91

Drug Delivery

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93

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95

ES

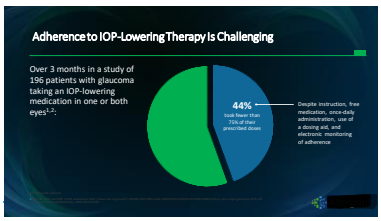
Adherence

96

And Now It's Time To Talk About Compliance!!!!!

This is so not Cool...

97



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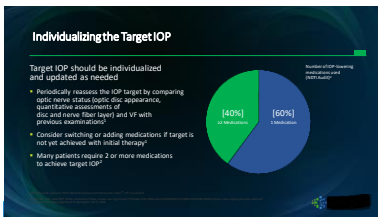

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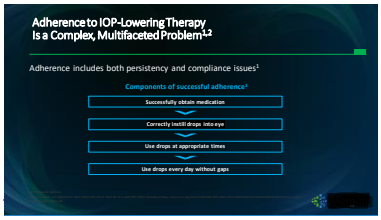


100

Compliance really is a hot topic

Dr David Friedman – OGF Educators Meeting 9/19

Looked at compliance studies in glaucoma- found that 70% compliance with medications was average

But is that good enough to preserve VF?

Friedman also showed that those who said they missed their drops some of the time… actually used their drops ~50% of the time.

That was much worse than those who say they never miss their drops

101

Predictors of Poor Adherence – Friedman 2019

Gaps In Visits

Patients Don't Understand Severity Of Disease

Cost of Drops (25%)

Those who Travel A Lot

Younger Pxs and Very Old Pxs

African-Americans

Those In Poor Health
- These drop adherence to <60%

102

Compliance, adherence and side effects of therapy

Compliance decreases the more bottles Rx'd

Robin – Each extra bottle used decreased compliance by 1/3

The more topical meds used the more ocular side effects occur

OSD in G pxs (way) higher than initially thought

60% of G pxs use ocular lubricants

103

What are the biggest barriers to proper compliance?

1. Forgetfulness

2. Ability to put drops in

3. Unaware of the importance of the drops

Cost was not in the top 5!!!

104

Ways To Improve Compliance

See Pxs more frequently… especially early in treatment

Improve tracking system – better identify no shows

Call/email appointment reminders

Reminders to pxs to take their drops

Change Dr/Patient intervention

G pxs ask 3.2 questions at visit whereas in other chronic diseases pxs ask ~ 6 questions/visit

105

106

MF

When Should Patients Return?

Managing Glaucoma

107

When Should Patients Return?

- Baseline period – making the diagnosis whether it is OHTN or Glaucoma
  - Important to have good quality visual fields and OCT as therapy is initiated
  - If therapy is initiated, then see 2-6 weeks afterwards
    - Making sure the medication/procedure is tolerated and effective
    - Having only one post therapy IOP measurement can be misleading
    - If not at target IOP, see sooner
  - Follow up period is for first year
  - If the person has mild to moderate glaucoma, examine every three months
    - Fields and imaging done at 6, 12, 18, 24 months
    - If stable and good quality can reduce interval for both doing fields/imaging and when to examine patient
- Stable vs. Uncontrolled

108

Ocular hypertension

- See on 6-month basis with imaging/fields done yearly
- May reevaluate over time

109

When Should Patients Return?

- Is there a need to do visual fields after the initial assessment if the patient is stable?
  - If OCT is stable, why do a field?
- Which fields to do?
  - 24-2 vs. 24-2C vs. 10-2
  - SITA Standard vs. Fast vs. Faster
  - What about bundling fields
    - Do 2 SITA Faster fields at one visit separating by few minutes

110

BG

Advancing Therapy

111

112

BG

Dry Eye and Glaucoma

113

114

Ocular Hypertension

- New risks are being discovered
  - Cigarette smoking
  - Alcohol
  - Time for menopause

115

The Risk of glaucoma after early bilateral oophorectomy

Abstract

116

Menopause exacerbates visual dysfunction in experimental glaucoma

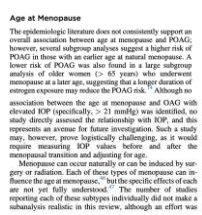
Abstract

117

The Association of Female Reproductive Factors with Glaucoma and Related Traits

A Systematic Review

118

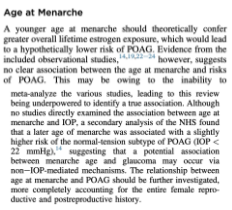


Age at Menopause

The epidemiologic literature does not consistently support an overall association between age at menopause and POAG; however, several subgroup analyses suggest a higher risk of POAG in those with an earlier age at natural menopause. A lower risk of POAG was also found in a large subgroup analysis of older women (> 65 years) who underwent menopause at a later age, suggesting that a longer duration of estrogen exposure may reduce the POAG risk.[3] Although no association between the age at menopause and OAG with elevated IOP (specifically, > 21 mmHg) was identified, no study directly assessed the relationship with IOP, and this represents an avenue for future investigation. Such a study may, however, prove logistically challenging, as it would require measuring IOP values before and after the menopausal transition and adjusting for age.

Menopause can occur naturally or can be induced by surgery or radiation. Each of these types of menopause can influence the age at menopause,[7] but the specific effects of each are not yet fully understood.[32] The number of studies reporting each of these subtypes individually did not make a subanalysis realistic in this review, although an effort was

119



Age at Menarche

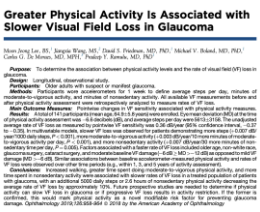
A younger age at menarche should theoretically confer greater overall lifetime estrogen exposure, which would lead to a hypothetically lower risk of POAG. Evidence from the included observational studies,[14,19,22–24] however, suggests no clear association between the age at menarche and risks of POAG. This may be owing to the inability to meta-analyze the various studies, leading to this review being underpowered to identify a true association. Although no studies directly examined the association between age at menarche and IOP, a secondary analysis of the NHS found that a later age of menarche was associated with a slightly higher risk of the normal-tension subtype of POAG (IOP < 22 mmHg),[14] suggesting that a potential association between menarche age and glaucoma may occur via non–IOP-mediated mechanisms. The relationship between age at menarche and POAG should be further investigated, more completely accounting for the entire female reproductive and postreproductive history.

120

ARTICLE OPEN

Association between lifestyle habits and glaucoma incidence: a retrospective cohort study

121



Greater Physical Activity Is Associated with Slower Visual Field Loss in Glaucoma

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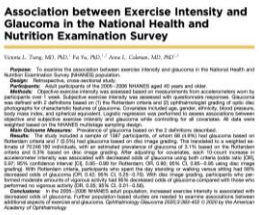


Association between Exercise Intensity and Glaucoma in the National Health and Nutrition Examination Survey

123

Smoking and progressive retinal nerve fibre layer thinning in glaucoma

124

125

Clinical and Epidemiologic Research

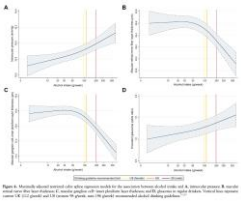
Alcohol Consumption, Genetic Risk, and Intraocular Pressure and Glaucoma: The Canadian Longitudinal Study on Aging

126

The Association of Alcohol Consumption with Glaucoma and Related Traits

Findings from the UK Biobank

127



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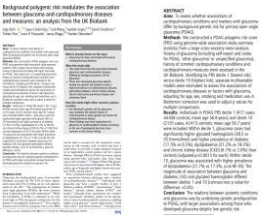
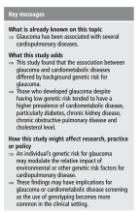


Background polygenic risk modulates the association between glaucoma and cardiopulmonary diseases and measures: an analysis from the UK Biobank

129



Key messages

What is already known on this topic

→ Glaucoma has been associated with several cardiopulmonary diseases.

What this study adds

→ This study found that the association between glaucoma and cardiometabolic diseases differed by background genetic risk for glaucoma.

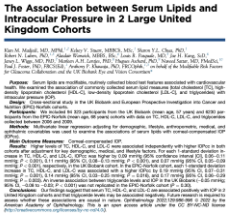
→ Those who developed glaucoma despite having low genetic risk tended to have a higher prevalence of cardiometabolic disease, particularly diabetes, chronic kidney disease, chronic obstructive pulmonary disease and cholesterol level.

How this study might affect research, practice or policy

→ An individual's genetic risk for glaucoma may modulate the relative impact of environmental or other genetic risk factors for cardiopulmonary disease.

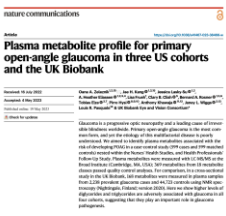
→ These findings may have implications for glaucoma or cardiometabolic disease screening as the use of genotyping becomes more common in the clinical setting.

130



The Association between Serum Lipids and Intraocular Pressure in 2 Large United Kingdom Cohorts

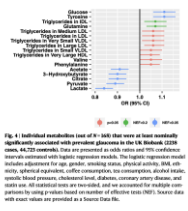
131



nature communications

Plasma metabolite profile for primary open-angle glaucoma in three US cohorts and the UK Biobank

132



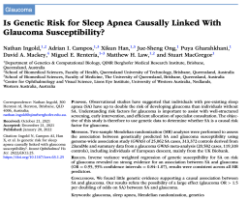
Glucose
Tyrosine
Triglycerides in VLDL
Glutamine
Triglycerides in Medium LDL
Triglycerides in LDL
Triglycerides in Very Large VLDL
Triglycerides in Large LDL
Triglycerides in Small VLDL
Triglycerides in Very Large HDL
Albumin
Phenylalanine
Acetate
3-Hydroxybutyrate
Citrate
Pyruvate
Lactate

0.8 0.9 1.0 1.1
OR (95% CI)

p<0.05 | FDR<0.2 | FDR<0.05

Fig. 4 | Individual metabolites (out of N = 168) that were at least nominally significantly associated with prevalent glaucoma in the UK Biobank (22356 cases, 44,720 controls). Data are presented as odds ratios and 95% confidence intervals estimated with logistic regression models. The logistic regression model includes adjustment for age, gender, smoking status, physical activity, BMI, ethnicity, spherical equivalent, coffee consumption, tea consumption, alcohol intake, systolic blood pressure, cholesterol level, diabetes, coronary artery disease, and statin use. All statistical tests are two-sided, and we accounted for multiple comparisons by using p-values based on number of effective tests (NET). Source data with exact values are provided as a Source Data file.

133



Glaucoma

Is Genetic Risk for Sleep Apnea Causally Linked With Glaucoma Susceptibility?

134

BMJ Open Association of sleep behaviour and pattern with the risk of glaucoma: a prospective cohort study in the UK Biobank

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Based on the UK Biobank data, this is the first large-prospective cohort study to comprehensively assess the association of sleep behaviours and patterns with glaucoma.

⇒ The application of cluster analyses (ie, multiple correspondence analysis (MCA) and a k-means clustering algorithm) enabled us to extract the most informative sleep patterns that inherently existed in the study population. Consequently, the exposed and reference groups in our analyses are realistic and mutually exclusive, leading to the most meaningful comparisons.

⇒ A wide range of important confounders were considered in the analyses since detailed information was available on sociodemographic factors, lifestyle, and somatic comorbidities.

⇒ The data were obtained from the UK Biobank but are not a representative sample of the entire-UK population. The generalisation of our findings to the entire UK or other populations needs further assessment.

135

BMC Medicine

RESEARCH ARTICLE Open Access

Associations of sleep apnoea with glaucoma and age-related macular degeneration: an analysis in the United Kingdom Biobank and the Canadian Longitudinal Study on Aging

Xikun Han, Samantha Sze-Yee Lee, Nathan Ingold, Nigel McArdle, Anthony P. Khawaja, Stuart MacGregor and David A. Mackey

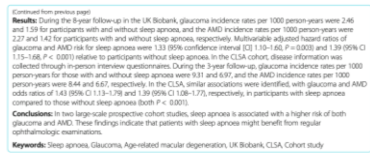
Abstract

Background: Sleep apnoea, a common sleep-disordered breathing condition, is characterised by upper airway collapse during sleep resulting in transient hypoxia, hypoperfusion of the optic nerve, and spike in intracranial pressure. Previous studies have reported conflicting findings on the association of sleep apnoea with glaucoma, and there are limited reports on the link between sleep apnoea and age-related macular degeneration (AMD).

Methods: Middle-aged and older participants from the longitudinal United Kingdom (UK) Biobank (n = 502,505) and the Canadian Longitudinal Study on Aging (CLSA; n = 24,073) were included in this analysis. Participants in the UK Biobank and the CLSA were followed for 8 and 3 years, respectively. Participants with diagnosed glaucoma or AMD at baseline were excluded from the analysis. In the UK Biobank, sleep apnoea and incident cases of glaucoma and AMD were identified through hospital inpatient admission, primary care records, and self-reported data. Multivariable Cox proportional hazards models were used to explore associations of sleep apnoea with incidence of glaucoma or AMD.

(Continued on next page)

136



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Results: During the 8-year follow-up in the UK Biobank, glaucoma incidence rates per 1000 person-years were 2.46 and 1.59 for participants with and without sleep apnoea, and the AMD incidence rates per 1000 person-years were 2.27 and 1.42 for participants with and without sleep apnoea, respectively. Multivariable adjusted hazard ratios of glaucoma and AMD risk for sleep apnoea were 1.33 (95% confidence interval [CI] 1.10–1.60, $P = 0.003$) and 1.39 (95% CI 1.15–1.68, $P < 0.001$) relative to participants without sleep apnoea. In the CLSA cohort, disease information was collected through in-person interview questionnaires. During the 3-year follow-up, glaucoma incidence rates per 1000 person-years for those with and without sleep apnoea were 9.31 and 6.97, and the AMD incidence rates per 1000 person-years were 8.44 and 6.67, respectively. In the CLSA, similar associations were identified, with glaucoma and AMD odds ratios of 1.43 (95% CI 1.13–1.79) and 1.39 (95% CI 1.08–1.77), respectively, in participants with sleep apnoea compared to those without sleep apnoea (both $P < 0.001$).

Conclusions: In two large-scale prospective cohort studies, sleep apnoea is associated with a higher risk of both glaucoma and AMD. These findings indicate that patients with sleep apnoea might benefit from regular ophthalmologic examinations.

Keywords: Sleep apnoea, Glaucoma, Age-related macular degeneration, UK Biobank, CLSA, Cohort study

137

Associations Between Niacin Intake and Glaucoma in the National Health and Nutrition Examination Survey

Précis: This study examined the association between dietary niacin intake and glaucoma in the 2005-2008 National Health and Nutrition Examination Survey (NHANES). Increased niacin intake was associated with lower odds of glaucoma overall and among women.

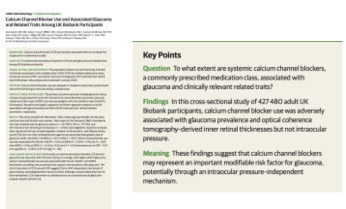
Purpose: To examine the association between dietary niacin intake and glaucoma in the 2005-2008 NHANES.

Materials and Methods: This cross-sectional study included adult participants of the 2005-2008 NHANES. The exposure was dietary niacin intake, which was examined as a continuous and categorical variable. The outcome was glaucoma as defined by regraded disc images. Covariates included age, sex, race/ethnicity, education level, income, body mass index, smoking status, alcohol use, cardiovascular disease, diabetes mellitus, daily energy intake, vitamin B2 and B6 consumption, and macular degeneration. Adjusting for all covariates, logistic regression was performed to examine the association between niacin intake and glaucoma in the overall population and stratified by sex.

Results: The weighted population included 5371 individuals (109,734,124 weighted), of whom 55 (1.0%) had glaucoma. Each 1 mg increase in niacin intake was associated with a 6% decreased odds of glaucoma odds [adjusted odds ratio (aOR) = 0.94, 95% CI = 0.90, 0.98]. Among women, increased niacin intake was associated with decreased odds of glaucoma both with niacin as a continuous (aOR = 0.89, 95% CI = 0.80, 0.99 per 1 mg increase in niacin intake) and binary variable (aOR = 0.35, 95% CI = 0.14, 0.90 for higher vs lower niacin intake).

Conclusions: In the 2005-2008 NHANES population, higher levels of niacin intake were associated with decreased odds of glaucoma overall and in women. Further studies are needed to examine the potential protective effects of niacin on glaucoma risk.

138



Calcium Channel Blocker Use and Associated Glaucoma and Related Traits Among UK Biobank Participants

Key Points

Question To what extent are systemic calcium channel blockers, a commonly prescribed medication class, associated with glaucoma and clinically relevant related traits?

Findings In this cross-sectional study of 427 480 adult UK Biobank participants, calcium channel blocker use was adversely associated with glaucoma prevalence and optical coherence tomography–derived inner retinal thicknesses but not intraocular pressure.

Meaning These findings suggest that calcium channel blockers may represent an important modifiable risk factor for glaucoma, potentially through an intraocular pressure–independent mechanism.

139

Thank You!!!

140