The Glaucoma Grab Bag:
Practical Guidelines for Effective Glaucoma Therapy

Danica J. Marrelli, OD, FAAO
University of Houston College of Optometry

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Financial Disclosure

- I have received I have received speaking or consulting fees from:
  - Allergan
  - Bausch & Lomb
  - Carl Zeiss Meditec
  - Ivantis
  - Santen

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Prostaglandin Analogs (PGs)

- Mechanism of action: increase uveosceral outflow
- Effect: excellent (25-35% reduction)
- Dosing: once daily (doesn't matter am/pm)
- Side effects:
  - Minimal systemic
  - Ocular:
    - Hyperemia
    - Hypertrichiasis
    - Hyperpigmentation – iris and periorbital skin
    - Prostaglandin-induced orbitopathy

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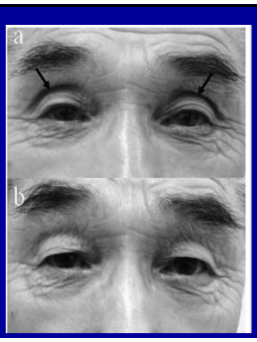

Optometry and Vision Science, Vol. 88, No. 9, September 2011

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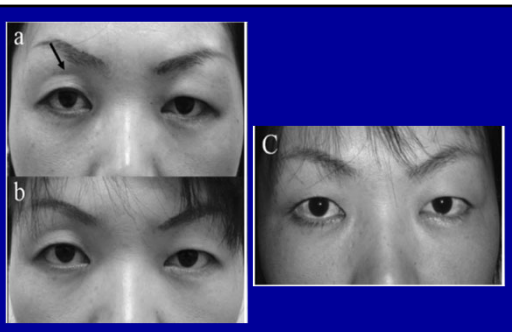

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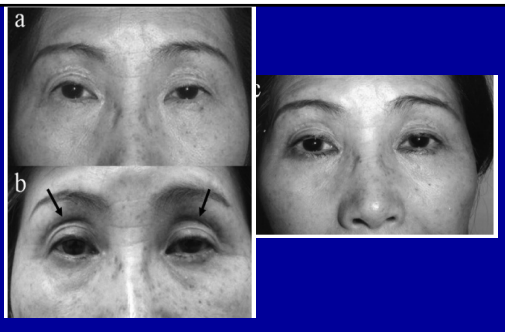

Optometry and Vision Science, Vol. 88, No. 9, September 2011

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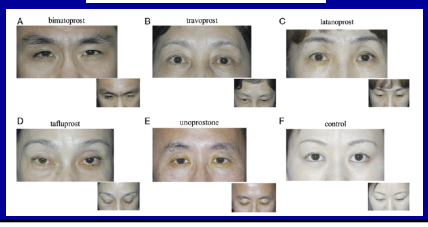
ORIGINAL STUDY

Deepening of the Upper Eyelid Sulcus Caused by 5 Types of Prostaglandin Analogs

Kenji Inoue, MD, PhD, Mineko Shiokawa, MD, PhD,* Manato Wakakura, MD, PhD,* and Goji Tomita, MD, PhD†*

J Glaucoma • Volume 00, Number 00, ■■ 2012



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Incidence of Prostaglandin-Induced Orbitopathy

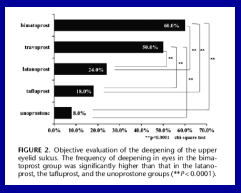

FIGURE 2. Objective evaluation of the deepening of the upper eyelid sulcus. The frequency of deepening in eyes in the bimatoprost group was significantly higher than that in the latanoprost, the tafluprost, and the unoprostone groups (**P<0.0001).

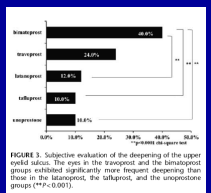

FIGURE 3. Subjective evaluation of the deepening of the upper eyelid sulcus. The eyes in the travoprost and the bimatoprost groups exhibited significantly more frequent deepening than those in the latanoprost, the tafluprost, and the unoprostone groups (**P<0.001).

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Glaucoma - Prostaglandins

- **When to Use**
  - **POAG**
  - **Pigmentary glaucoma**
  - **Pseudoexfoliation glaucoma**
  - **Normal tension glaucoma**
  - **Ocular Hypertension**

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Glaucoma - Prostaglandins

- **When to reconsider:**
  - **Acute rise in IOP**
    - **Acute angle closure**
    - **Posner-Schlossman syndrome**
    - **Post-surgical spike**
  - **Pt with history of CME or risk of CME**
  - **Unilateral therapy**
  - **Pregnancy**
  - **Uveitic glaucoma (???)**
  - **Neovascular glaucoma (???)**

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UVEITIS

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Am J Ophthalmol. 2008 Dec;146(6):876-82.

Flare-up rates with bimatoprost therapy in uveitic glaucoma.

Fortuna E, Cervantes-Castañeda RA, Bhat P, Doctor P, Foster CS.
Massachusetts Eye Research and Surgery Institute, Cambridge, Massachusetts 02142, USA.

Erratum in:
Am J Ophthalmol. 2009 Mar;147(3):565. Castañeda-Cervantes, Rene A [corrected to Cervantes-Castañeda, Rene A].

Abstract

PURPOSE: To evaluate the rate of flares in patients with uveitic glaucoma treated with topical bimatoprost and to assess its effect on intraocular pressure (IOP) in this subset of patients.

DESIGN: Retrospective case series.

METHODS: All patients seen at one subspecialty uveitis practice with history of uveitic glaucoma treated with topical bimatoprost were identified and the data collected, which included onset, type, duration of uveitis, onset of secondary glaucoma, and previous therapies for glaucoma. The time of onset of bimatoprost therapy, the IOP, and flare-up rate before and after initiation of treatment with bimatoprost were recorded at one week and one, three, and six months of follow-up.

RESULTS: Of the 42 patients (59 eyes) identified, 12 patients had used other topical lipid agents, which were replaced by bimatoprost. Twenty-three patients had not used any lipid agents and bimatoprost was added to their existing antiglaucoma regimen. Seven patients were newly diagnosed with uveitic glaucoma and were commenced with topical bimatoprost. The rate of uveitis flares while on other antiglaucoma therapy was 52 per 100 person-years follow-up, while on bimatoprost therapy it was 32.4 per 100 person-years follow-up (P = .206). The mean IOP prior to bimatoprost therapy was 27 +/- 13.2 mm Hg and after initiation of topical bimatoprost was 15 +/- 5.5 mm Hg at the end of six months (P = .0008).

CONCLUSION: These data suggest that bimatoprost is an effective IOP-lowering agent in patients with uveitic glaucoma in whom the uveitis is controlled on immunomodulatory therapy, and it does not increase the rate of flares of uveitis in these patients.

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Br J Ophthalmol. 2008 Jul;92(7):916-21. Epub 2008 May 6.

Use of ocular hypotensive prostaglandin analogues in patients with uveitis: does their use increase anterior uveitis and cystoid macular oedema?

Chang JH, McCluskey P, Missotten T, Ferrante P, Jalaludin B, Lightman S.

Department of Clinical Ophthalmology, Institute of Ophthalmology, Moorfields Eye Hospital, City Road, London, UK.

Abstract

AIM: A retrospective comparative case series was studied to determine whether the use of prostaglandin (PG) analogues to treat raised intraocular pressure (IOP) in patients with uveitis resulted in an increase in the frequency of anterior uveitis or cystoid macular oedema (CMO).

METHODS: 163 eyes of 84 consecutive patients with uveitis and raised IOP treated with a PG analogue at two tertiary referral uveitis clinics were identified over a 3-month period. Control eyes were selected as those uveitic eyes of the same patients, which were treated with topical IOP-lowering agent(s) other than a PG analogue. Pretreatment IOP was compared with the mean IOP during PG analogue treatment. The frequency of anterior uveitis and CMO during PG analogue treatment was compared with the frequency of these complications in the control eyes during non-PG IOP-lowering treatment.

RESULTS: Significant IOP reductions were observed during PG analogue treatment. There was no significant difference in the frequency of anterior uveitis in those eyes treated with PG analogues and those treated with non-PG agents ($p = 0.87$, Fisher exact test). None of the 69 uveitic eyes without a previous history of CMO developed this complication. There was no increase in the frequency of visually significant CMO during PG treatment compared with that during non-PG treatment ($p = 0.19$, Fisher exact test).

CONCLUSION: This study demonstrates that PG analogues are potent topical medications for lowering raised IOP in patients with uveitis and are not associated with increased risk of CMO or anterior uveitis.

⊕ Publication Types, MeSH Terms, Substances

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PubMed.gov — US National Library of Medicine, National Institutes of Health

PubMed | Advanced

Abstract | Send to:

Graefes Arch Clin Exp Ophthalmol. 2009 Jun;247(6):775-80. doi: 10.1007/s00417-009-1036-3. Epub 2009 Jan 28.

Efficacy and safety of latanoprost in eyes with uveitic glaucoma.

Markomichelakis NN[1], Kostakou A, Halkiadakis I, Chalkiadis S, Papakonstantinou D, Georgopoulos G

⊕ Author information

Abstract

BACKGROUND: To compare the efficacy and safety of latanoprost against a fixed combination of dorzolamide and timolol in eyes with elevated intraocular pressure (IOP) or glaucoma and anterior or intermediate uveitis.

METHODS: Fifty-eight patients with anterior or intermediate uveitis and elevated IOP or glaucoma presented or followed up in the Ocular Inflammation and Immunology Service of General Hospital of Athens were randomly assigned to receive treatment either with latanoprost (30) or with dorzolamide/timolol (28). The main outcome measures were inflammatory relapses and IOP response to treatment.

RESULTS: Ten patients (34%) in the latanoprost group and sixteen patients (57%) in the dorzolamide/timolol group experienced relapses of anterior uveitis ($p = 0.93$). There was no statistical difference between the two groups in respect of inflammatory relapses ($p = 0.21$). Twenty-one patients were followed up before starting latanoprost. The number of recurrences of anterior uveitis per patient per year before treatment with latanoprost was 0.82 +/- 1.2. The rate of relapses per patient per year after starting latanoprost was 0.39 +/-0.7 for these patients ($p = 0.038$). After 1 year of treatment, intraocular pressure was dropped from 27.8 +/- 8.4 mmHg to 18.6 +/- 5.3 mmHg ($p < 0.001$) in the latanoprost group and from 28.2 +/-8.1 mmHg to 22.6 +/-10.1 mmHg ($p < 0.001$) in the dorzolamide/timolol group. Four patients during treatment with latanoprost and five patients during

CONCLUSION: Latanoprost is safe and equally effective to a fixed combination of dorzolamide and timolol in the treatment of uveitic glaucoma.

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The Use of Prostaglandin Analogs in the Uveitic Patient

Michael B. Horsley and Teresa C. Chen

Glaucoma Service, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA, USA

Seminars in Ophthalmology, 26(4-5), 285–289, 2011

SUMMARY

The use of prostaglandin analogs in uveitic patients remains controversial. A causal relationship has yet to be established between prostaglandins and the reactivation of anterior uveitis, the development of cystoid macular edema, or the reactivation of HSK.

Due to the efficacy of prostaglandins in lowering IOP in patients with uveitis and the small likelihood of developing these rare complications, prostaglandin analogs should remain in the treatment algorithm of uveitic glaucoma patients.

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Cystoid Macular Edema
following cataract surgery

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J Ophthalmol. 2010;2010:690707. Epub 2010 Nov 7.

Prostaglandin-induced cystoid macular edema following routine cataract extraction.

Agange N, Mosead S.

Department of Ophthalmology, University of California, Irvine, CA 92697, USA.

Abstract

To our knowledge, we are reporting the first case of a 59-year-old man who developed recurrent CME with three separate trials of three different prostaglandin class drugs following uncomplicated phacoemulsification with intraocular lens implantation. Despite multiple reports of individual prostaglandin (PG) analogues being suggested as the cause of CME, there are no recommendations regarding withholding these medications in the perioperative period. Our patient first developed CME OD 4-months post uncomplicated cataract extraction. XALATAN (Latanoprost) had been restarted after surgery and discontinued at onset of CME. While off XALATAN (Latanoprost), the patient's CME resolved, but his IOP rose. The patient was started on LUMIGAN (Bimatoprost) to control the IOP, but within weeks his CME recurred. The patient's CME was again treated and his IOP remained acceptable, but then progressively increased. TRAVATAN (Travoprost) was attempted, but he presented with a third round of CME. Definitive conclusions about causal relationships cannot be made without well-designed, prospective clinical trials addressing this issue.

PMID: 21076526 [PubMed - in process] PMCID: PMC2975071 Free PMC Article

⊕ LinkOut - more resources

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Clinically Significant Diabetic Macular Edema???

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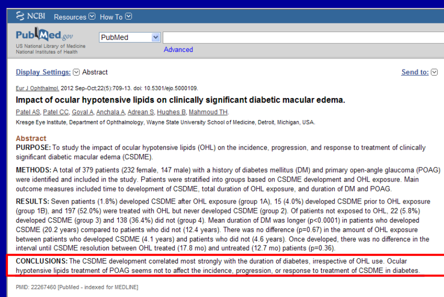

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Eur J Ophthalmol. 2012 Sep-Oct;22(5):709-13. doi: 10.5301/ejo.5000109.

Impact of ocular hypotensive lipids on clinically significant diabetic macular edema.

Patel AS, Patel CC, Goyal A, Anchala A, Adrean S, Hughes B, Mahmoud TH.

Kresge Eye Institute, Department of Ophthalmology, Wayne State University School of Medicine, Detroit, Michigan, USA.

Abstract

PURPOSE: To study the impact of ocular hypotensive lipids (OHL) on the incidence, progression, and response to treatment of clinically significant diabetic macular edema (CSDME).

METHODS: A total of 379 patients (232 female, 147 male) with a history of diabetes mellitus (DM) and primary open-angle glaucoma (POAG) were identified and included in the study. Patients were stratified into groups based on CSDME development and OHL exposure. Main outcome measures included time to development of CSDME, total duration of OHL exposure, and duration of DM and POAG.

RESULTS: Seven patients (1.8%) developed CSDME after OHL exposure (group 1A), 15 (4.0%) developed CSDME prior to OHL exposure (group 1B), and 197 (52.0%) were treated with OHL but never developed CSDME (group 2). Of patients not exposed to OHL, 22 (5.8%) developed CSDME (group 3) and 138 (36.4%) did not (group 4). Mean duration of DM was longer (p<0.0001) in patients who developed CSDME (20.2 years) compared to patients who did not (12.4 years). There was no difference (p=0.67) in the amount of OHL exposure between patients who developed CSDME (4.1 years) and patients who did not (4.6 years). Once developed, there was no difference in the interval until CSDME resolution between OHL treated (17.8 mo) and untreated (12.7 mo) patients (p=0.36).

CONCLUSIONS: The CSDME development correlated most strongly with the duration of diabetes, irrespective of OHL use. Ocular hypotensive lipids treatment of POAG seems not to affect the incidence, progression, or response to treatment of CSDME in diabetes.

PMID: 22267460 [PubMed - indexed for MEDLINE]

C36

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Glaucoma - Prostaglandins

- **Drugs:**
  - **latanoprost (Xalatan® and generic, Xelpros ®)**
  - **travoprost (Travatan-Z ® and generic)**
  - **bimatoprost (Lumigan ® 0.01% and generic 0.03%)**
  - **tafluprost (Zioptan ®)**
- **How do they compare?**
  - **Efficacy**
  - **Side effects**
  - **Cost**

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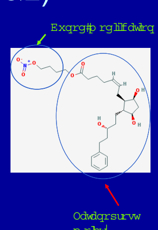
Latanoprostene Bunod (Vyzulta®, B&L)

- Latanoprostene = latanoprost
  - Increases uveoscleral outflow
- Bunod modification donates NO
  - Exerts its effect in trabecular smooth muscle
  - Activating cyclic guanosine monophosphate signaling pathway
  - Resulting in trabecular relaxation and increased conventional outflow
- Mechanisms would be expected to be additive



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Latanoprostene Bunod vs Timolol: APOLLO and LUNAR Trials

- Study design
  - Randomized (2:1 [LBN:timolol]) phase 3, multicenter, double-masked, parallel-group studies
- 2 treatment groups
  - LBN, 0.024%, qhs
  - Timolol, 0.5%, bid

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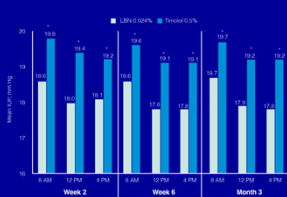
APOLLO: Efficacy and Safety

- IOP reductions
  - 8 to 9 mm Hg for LBN (n = 264)
  - 6.5 to 7.5 mm Hg for timolol (n = 123)
- Adverse events
  - Similar rates between groups
  - Most common:
    - Eye irritation
    - Conjunctival hyperemia



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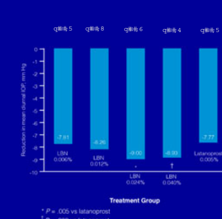
Phase 2 Study of Latanoprostene Bunod vs Latanoprost: VOYAGER

- N = 413 (intent to treat)
- At highest doses, LBN lowered IOP 1 to 1.5 mm Hg more than latanoprost
- Most common adverse event: pain upon instillation
- Conjunctival or ocular hyperemia:
  - LBN: 7.0%
  - Latanoprost: 8.5%



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Slide 22

C36 new info, inc citation
Cynthia, 7/14/2016

Glaucoma – beta-adrenergic antagonists (beta blockers)

- Mechanism of action: decrease aqueous production
- Efficacy: very good (25-30% reduction)
- Dosing: once vs twice daily
- Side effects:
  - Minimal ocular side effects
  - Systemic:
    - Bradycardia
    - Bronchial constriction
    - ** CHECK EXISTING MEDS, VITALS
- Short term escape & long term drift

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Lack of Long-Term Drift in Timolol's Effectiveness in Patients with Ocular Hypertension

Rod Bengtsson and Anders Heijl

CONCLUSIONS. In agreement with other masked and controlled studies and in conflict with uncontrolled ones, the present study did not demonstrate long-term drift of intraocular pressure in patients with ocular hypertension treated with topical timolol. (*Invest Ophthalmol Vis Sci.* 2001;42:2839–2842)

Investigative Ophthalmology & Visual Science, November 2001, Vol. 42, No. 12

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Glaucoma – beta blockers

- When to use:
  - First line therapy for patients with contraindications to prostaglandins
  - Need rapid lowering of IOP
  - Cost (generic is cheap)
  - Added drug for prostaglandin users
    - Different mechanism of action
- When to reconsider:
  - Symptomatic bradycardia
  - CHF patient
  - Patient on oral bb (+/-)
  - Normal tension glaucoma

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Glaucoma – beta blockers

- Available drugs:
  - timolol maleate (Timoptic®, Timoptic-XE ®, Timoptic PF®, generics, Istalol ®)
  - timolol hemihydrate (Betimol ®)
  - levobunolol (Betagan ® and generic)
  - metipranolol (Optipranolol ® and generic)
  - carteolol (Ocupress ® and generic)
  - betaxolol (generic solution, Betoptic-S ®)

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Glaucoma – alpha-adrenergic agonist

- Mechanism of action:
  - Decrease in aqueous production
  - Increase in uveoscleral outflow
- Efficacy: good (20-25% reduction)
- Dosing: tid vs bid
- Side effects:
  - Systemic:
    - Somnolence
    - Dry mouth
    - Dizziness/fainting
  - Ocular:
    - allergy

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Glaucoma - brimonidine

- Allergy:
  - Original brimonidine ® 0.2% generic
    - 30%+ allergy rate
  - Alphagan-P 0.15% (only available in "generic" with Polyquad ® preservative)
    - 20% allergy rate
  - Alphagan-P ® 0.1% (Purite ® preservative)
    - 10-15% allergy rate
  - Combigan ® (0.2%, with 0.5% timolol, BAK)
    - 5% allergy rate (?)
  - Simbrinza® (0.2% with 2% dorzolamide, BAK) -- ??? Allergy rate

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Glaucoma - brimonidine

- When to use
  - Excellent additivity with prostaglandin
  - Good additivity with beta-blocker
  - Rapid IOP lowering (esp in combo)
  - Preservative toxicity/allergy
  - Category B pregnancy (D/C in breastfeeding)
- When to reconsider
  - Monotherapy (dosing)
  - Hx of allergy (any form of brimonidine)
  - CHILDREN (contraindication)

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A Randomized Trial of Brimonidine Versus Timolol in Preserving Visual Function: Results From the Low-pressure Glaucoma Treatment Study

THEODORE KRUPIN, JEFFREY M. LIEBMANN, DAVID S. GREENFIELD, ROBERT RITCH, AND STUART GARDINER, ON BEHALF OF THE LOW-PRESSURE GLAUCOMA STUDY GROUP

AMERICAN JOURNAL OF OPHTHALMOLOGY

APRIL 2011

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LoGTS

- Randomized, double-masked clinical trial to compare brimonidine 0.2% vs timolol 0.5% in preserving visual function in normal tension glaucoma patients
  - brimonidine 0.2% bid
  - timolol maleate 0.5% bid
  - Followed with VF every 4 months for minimum of 4 years

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LoGTS

- Results:
  - No significant difference in IOP
  - Significant dropout in brimonidine group (allergy)
  - Significan/dramatic difference in visual field progression
    - 9% for brimonidine group
    - 39% for timolol group
- Question: what does this mean?

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Glaucoma – carbonic anhydrase inhibitors

- Mechanism of action: decreased aqueous production
- Efficacy: excellent (oral – 40-50%+); good (topical – 15-20%)
- Dosing: bid – tid
- Side effects:
  - Topical:
    - Bitter taste
    - Stinging
    - Hyperemia
    - Corneal endothelium

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Glaucoma - CAIs

- When to consider:
  - Good addition to prostaglandin
  - Brimonidine allergy
- When to avoid:
  - Fuchs corneal endothelial dystrophy
  - Pregnancy
  - Sulfa allergy (???)
- Available:
  - Dorzolamide (Trusopt® and generic)
  - Brinzolamide (Azopt®)
  - dorzolamide/timolol (Cosopt®, Cosopt PF®, and generic)
  - dorzolamide/brinzolamide (Simbrinza®)

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JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS
Volume 29, Number 5, 2013
© Mary Ann Liebert, Inc.
DOI: 10.1089/jop.2012.0123

Evaluation of Adverse Events in Self-Reported Sulfa-Allergic Patients Using Topical Carbonic Anhydrase Inhibitors

Guilherme B. Guedes,[1] Abraar Karan,[1] Hylton R. Mayer,[2] and M. Bruce Shields[1]

Conclusion: It may be safe to use a topical CAI in patients who report a history of a sulfa allergy. Patients with medication allergies of any kind may be more likely to develop allergic reactions to other, unrelated drug classes.

diagnosis of glaucoma. The outcome measure was the development of an adverse reaction (ocular, systemic, or both) within at least 30 days after receipt of 1 of 4 classes of topical glaucoma medications: CAIs (dorzolamide and brinzolamide), prostaglandin analogues, beta-adrenergic blockers, and alpha2-adrenergic agonists.

Results: Patients with a self-reported history of sulfa allergy had significantly more ocular adverse reactions after the initiation of any of the topical antiglaucoma medications when compared to those patients with no reported allergies. Patients with a self-reported sulfa allergy and patients who self-reported other, nonsulfa-related allergies had similar rates of adverse reactions to most of the topical medications. The patients reporting a sulfa allergy who used topical CAIs did not have more adverse reactions compared with patients who reported having other, nonsulfa-related allergies who used topical CAIs. Self-reported sulfa-allergic patients had similar rates of adverse reactions to topical CAIs compared with topical prostaglandin analogues.

Conclusion: It may be safe to use a topical CAI in patients who report a history of a sulfa allergy. Patients with medication allergies of any kind may be more likely to develop allergic reactions to other, unrelated drug classes.

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Sulfonamide cross-reactivity: Is there evidence to support broad cross-allergenicity?

NICOLE R. WULF AND KARL A. MATUSZEWSKI

Purpose. Published and manufacturer-provided data regarding potential cross-reactivity between antibacterial and nonantibacterial sulfonamide agents are reviewed.

Summary. An estimated 3–6% of the general population is allergic to sulfonamides and thus at risk for type I and other hypersensitivity reactions to sulfamethoxazole and other sulfonamide antibacterial agents. Concerns have been raised that a history of sulfa allergy may be associated with an increased risk of adverse reactions to a wide range of nonantibacterial sulfonamides, including certain antivirals, carbonic anhydrase inhibitors, cyclooxygenase-2-selective nonsteroidal antiinflammatory drugs, loop and thiazide diuretics, and sulfonylureas; concerns have also been raised that patients who have experienced an allergic reaction to one nonantibacterial sulfonamide may be at risk for an adverse reaction to others. Structurally, none of the nonantibiotic sulfonamides exhibit both of the features shown to be responsible for sulfonamide reactions (i.e., an N-containing ring attached to the N1 nitrogen of the sulfonamide group and an arylamine group at the N4 position), and only two agents (amprenavir and fosamprenavir) have the latter characteristic. A comprehensive literature search (1966–December 2011) identified nine case reports indicating possible cross-reactivity to sulfonamide medications; however, in most cases, adequate patient testing was not conducted to firmly establish either sulfa allergy or sulfonamide cross-sensitivity. The weight of evidence suggests that withholding nonantibacterial sulfonamides from patients with prior reactions to antibacterial sulfonamides or other nonantibacterial sulfonamides is not clinically justified.

Conclusion. A review of the professional literature and manufacturer-provided data did not find convincing evidence of broad cross-reactivity between antibacterial and nonantibacterial sulfonamide agents.

Am J Health-Syst Pharm. 2013; 70:1487-94

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Glaucoma - acetazolamide

- **Typically used in emergency/acute situations rather than long term due to systemic side effects:**
  - **Paresthesia**
  - **Kidney stones**
  - **Metabolic acidosis**
  - **Blood dyscrasia**
- **Typical use:**
  - **Post-surgical IOP elevation**
  - **Acute angle closure (PUPILLARY BLOCK ONLY)**
  - **Extremely elevated IOP**
- **Dosing:**
  - **250 mg tablets qid (generic)**
  - **500 mg time-released capsules (Sequels ®, generic) bid**

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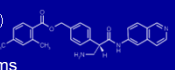
(NEW-ish DRUG) Rho-Kinase Inhibitors

- netarsudil (Rhopressa®, Aerie) FDA approved in December 2017, in pharmacies Spring 2018
  - Inhibits the enzyme Rho kinase
  - Also inhibits norepinephrine transporter (increases adrenergic activity)



- Potentially lowers IOP by 3 mechanisms
  - Increasing trabecular meshwork outflow
  - Reducing episcleral venous pressure
  - Reducing aqueous production (via norepinephrine transporter inhibition)

IOP = (PRODUCTION/OUTFLOW) +EVP

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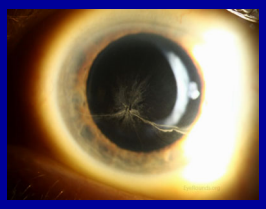
Netarsudil (Rhopressa®)

- Dosing is once daily (p.m.)
- Side Effects:
  - Hyperemia
    - 50-60% of patients
    - Sporadic
  - Conjunctival hemorrhages (small)
  - Corneal verticillata
    - Intracellular phospholipids
    - Asymptomatic
    - Did not decrease visual function



41

Netarsudil (Rhopressa)

- Lowered IOP approximately 5-7 mmHg, irrespective of starting IOP
  - May be best suited for those with lower IOP (?)
- Current development plan is in combination with latanoprost
  - netarsudil, 0.02%, plus latanoprost fixed combination lowered IOP more than latanoprost ($P < .0001$) or netarsudil, 0.02% ($P < .0001$), did in a completed phase 2b trial
  - Hyperemia: 14% latanoprost, 40% netarsudil, 40% fixed combination

42

NEW(ish) DRUG!!!!
latanoprost + netarsudil (Rocklatan)

- First available fixed combination in US with a pga
- First available fixed combination with once daily dosing (night)
- May be particularly effective in patients with lower starting IOP
- FDA approved March 2019

43

Glaucoma - pilocarpine

- **Mechanism of action – increase trabecular outflow**
- **Efficacy: good (25%)**
- **Dosing: qid**
- **Side effects:**
  - **Accommodative spasm**
  - **Browache**
  - **Bronchial constriction**
- **Use: acute angle closure with pupillary block (low concentration)**

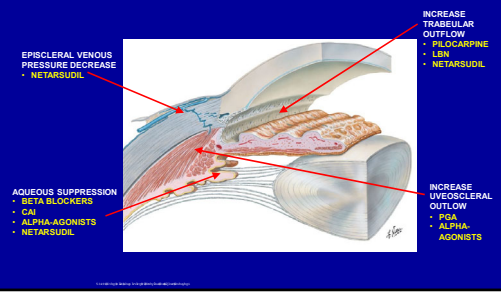
44

Glaucoma - pilocarpine

- Avoid:
  - Inflammatory
  - Neovascular
  - "Posterior Pushing" secondary angle closure (ex: topiramate-induced angle closure)

45

IOP-Lowering Drugs: Sites of Action



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Fixed Combination Medications

- dorzolamide/timolol (Cosopt® and generic; Cosopt PF®)
  - Bid dosing
- brimonidine/timolol (Combigan®)
  - 5% allergy rate
  - Bid dosing
- brinzolamide/brimondine (Simbrinza®)
  - First non-beta blocker fixed combination
  - BAK-preserved
  - TID dosing
- Netarsudil/Latanoprost (Rocklatan ®)
  - First pga fixed combo in US
  - Qhs dosing

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Other Fixed Combinations

- Imprimis Pharmacy:
  - Compound multiple formulations of off-patent ophthalmics in a multi-dose preservative-free bottle, sell directly to patient (no insurance)
  - Potential Advantages:
    - No preservatives
    - Multiple drugs in one bottle = better adherence
    - Potential cost savings
    - Eliminates third-party dictated prescribing

48

Generic Grab Bag

- timolol maleate, other BBs
- latanoprost –or- travoprost – or – bimatoprost 0.03%
- brimonidine 0.15% -or- 0.2%
- dorzolamide
- (dorzolamide/timolol)

Generic MMT:

- Latanoprost or travoprost or bimatoprost
- Brimonidine 0.15% or 0.2%
- Dorzolamide/timolol combo

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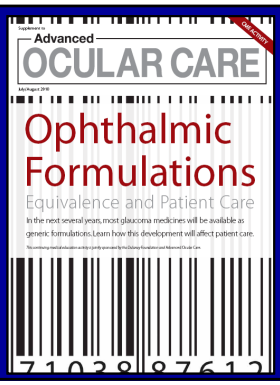

50

BAK-free Grab Bag

- Timoptic PF ®
- Travatan-Z ®, Xelpros® or Zioptan ®
- brimonidine 0.15% -or- Alphagan-P ® 0.1%
- Cosopt PF®

- BAK-free MMT:
  - Xelpros, Travatan Z, or Zioptan
  - Brimonidine 0.15% or 0.2%
  - Cosopt PF

53

- To gain FDA approval, a generic drug must:
  - Contain the same *active* ingredient
  - Be identical in strength, dose form, and route of administration
  - Be bioequivalent (80-120% of branded product)
    - Not the same thing as therapeutic effect
  - Have the same indications for use
  - Meet the same batch requirements for identity, strength, purity, and quality
  - Have a similar shelf life

51

- We don't know about:
  - Loss of control with long term use
  - Tolerability
  - Efficacy
- Multiple companies can make a generic; differences may not be apparent on bottle
- Cannot know for sure which company the pharmacy will have
- Patient's confidence in generics varies
- Somewhat difficult to understand efficacy due to slow nature of disease

52

Preservative-free Grab Bag

- Timoptic PF ®
- Zioptan ®
- Cosopt PF ®
- (Compounded Drugs)

- Preservative-free MMT
  - Cosopt PF
  - Zioptan

54

Medication Follow-Up Questions

1. Is patient using drug?
2. Is patient tolerating drug?
3. Is there a therapeutic effect?
4. Am I reaching target IOP?

55

POLLING QUESTION

What do you do if a pga works but is not enough?

A. Refer for SLT
B. Refer for consultation
C. Add a BB
D. Add brimonidine
E. Add CAI
F. Switch to Rocklatan

56

POLLING QUESTION

What do you do if a pga is NOT effective?

A. Refer for SLT
B. Switch to different pga
C. Add BB
D. Add brimonidine
E. Add CAI
F. Switch to Rocklatan
G. None of the above

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TYPICAL DRUG STEPPING

- Start with PGA
  - If good therapeutic effect but NOT reaching target, add timolol, brimonidine, or topical CAI
    - If good therapeutic effect with 2nd drug but still NOT reaching target, switch 2nd drug to combo
    - ***Here is where Vyzulta or Rocklatan could work
  - If PGA not having a good therapeutic effect
    - Consider non-adherence; re-try for another month
    - Consider switch to branded if using generic
    - Consider switching class (BB)
      - Can easily switch BB to combo if need additional therapy
  - If multiple meds don't work - COMPLIANCE

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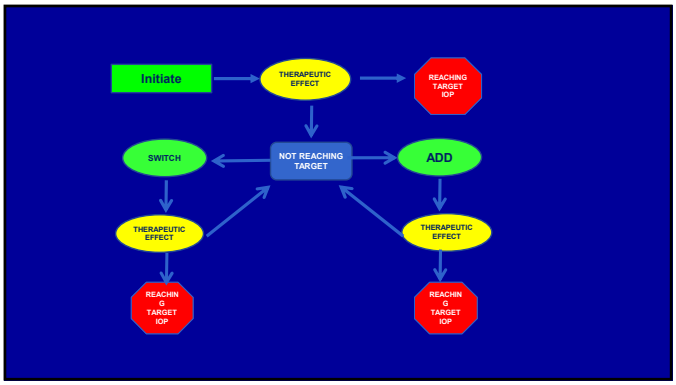

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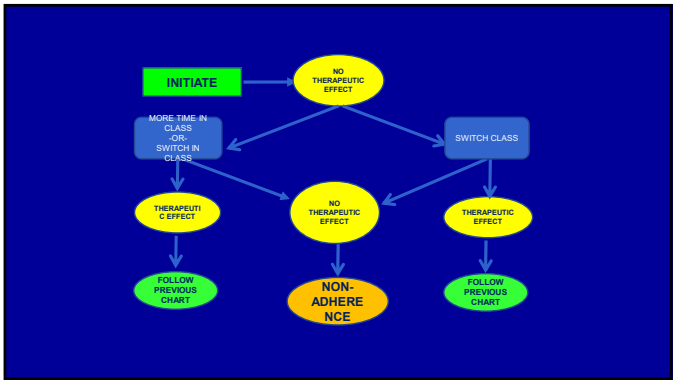


60

Example: Guillermo

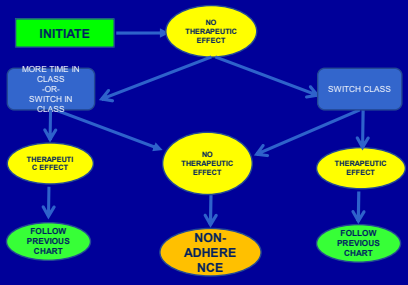
- 61yo healthy HM
- High risk ocular hypertension
  - IOPs range 28-32 OD, OS (multiple visits)
  - CCT 500 OU
  - C/D 0.4 OD, OS; normal, no RNFLDO
  - VF normal OU
  - OCT normal OU
- Goal IOP: 20% reduction from highest = under 25mmHg
- Initial therapy: latanoprost qhs OU

61

Example: Guillermo

- Follow-up:
  1. Is patient using drug? YES, claims excellent compliance
  2. Is patient tolerating drug? YES, minor redness, otherwise fine.
  3. Is there a therapeutic effect? NO – 20% minimum expected from first line med. His IOP on follow-up is 28mmHg
  4. Meeting target? (NO)

62



63

Example: Guillermo

- Tried additional time: No change in IOP
- Switched to branded: No change in IOP
  - COMPLIANCE CHECK!!!!
    - Pt adamant that he is using properly
    - Observe drop instillation = good technique
- Switched to timolol: IOP 21mmHg OD, 18mmHg OS

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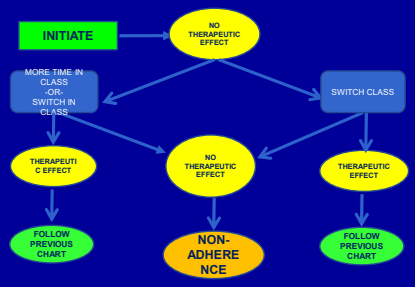


65

Example: Natalie

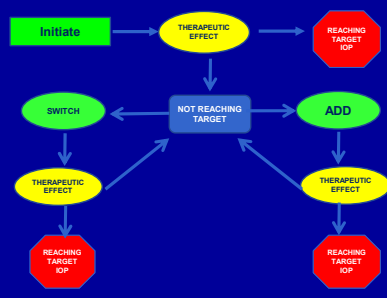
- 62yo Indian female with moderate POAG
  - IOP range 23-27mmHg OU
  - C/D ratio 0.8 OD, OS
  - Mild VF defect consistent with disc appearance
  - Ocular history also includes mild Fuchs corneal endothelial dystrophy
  - Medical history unremarkable
  - GOAL IOP: 35% reduction from highest = 17mmHg or less (mid teens)
  - Initial therapy: latanoprost

66

Example: Natalie

- Follow-up:
  1. Is patient using drug? YES, claims excellent compliance
  2. Is patient tolerating drug? YES
  3. Is there a therapeutic effect? YES – 20% minimum expected from first line med (<21). Pt's IOP on meds = 20
  4. Meeting target? NO – Target is 17mmHg or less

67



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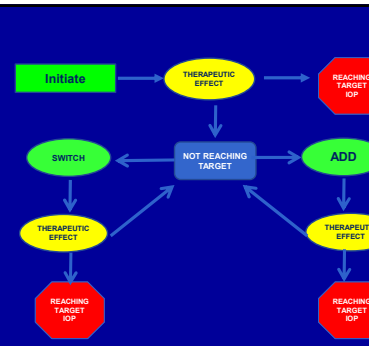
Example: Natalie

- Choices:
  - Add
    - CAI (but remember Fuch's)
    - BB
    - Brimonidine
  - Switch
    - PGA + timolol
    - Timolol alone
    - Other single or FDC
- We went with brimonidine
  - On return, IOP 18mmHg

69



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Glaucoma Drugs: What's Next?

- Drug Delivery System (DDS)
  - Contact lens delivery
  - Punctal plug delivery
  - Insertable
  - Injectable
    - Sub-conjunctival
    - Anterior chamber
    - vitreous

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Where Does Laser Fit In?

73

SELECTIVE LASER TRABECULOPLASTY

- Specially designed laser used to treat pigmented trabecular meshwork cells
- Application of laser is same technique as for Argon Laser Trabeculoplasty (ALT)
- Differences:
  - Very short pulse (3 nanoseconds)
  - Eliminates collateral "burn" damage
  - Mechanism appears to be cytokine-mediated macrophage recruitment
  - Can be repeated

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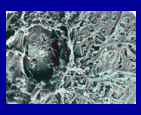
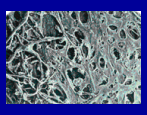
SELECTIVE LASER TRABECULOPLASTY



ALT



SLT

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SELECTIVE LASER TRABECULOPLASTY

- Post-Op Care
  - Similar to ALT (? Steroid, ? NSAID)
- Complications:
  - Similar to ALT
  - Include:
    - Corneal abrasion
    - Uveitis
    - Scattered PAS
    - Transient IOP rise

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"Selective Laser Trabeculoplasty as Primary Treatment for Open Angle Glaucoma" (Archives Ophthalmology July 2003)

- 45 eyes treated with SLT as primary treatment
- Mean IOP decrease: 7.7 mmHg (+/- 3.5)
- 4% non-response to treatment
- 3 eyes required meds at end of 18 month follow up
- Complications: redness, IOP spike

77

SELECTIVE LASER TRABECULOPLASTY

Ayala M, Chen E. Long-Term Outcomes of Selective Laser Trabeculoplasty (SLT) Treatment. Open Ophthalmol J. 2011;5:32-4. Epub 2011 May 12.

- **Retrospective chart review of 120 eyes of 120 patients undergoing 90° SLT**
- **Primary measure: time to failure**
- **Results:**
  - **Average time to failure: 18 months**
  - **Success at 12 months: 62%**
  - **Success at 24 months: 34%**
  - **Success at 36 months: 28%**
  - **Success at 48 months: 24%**

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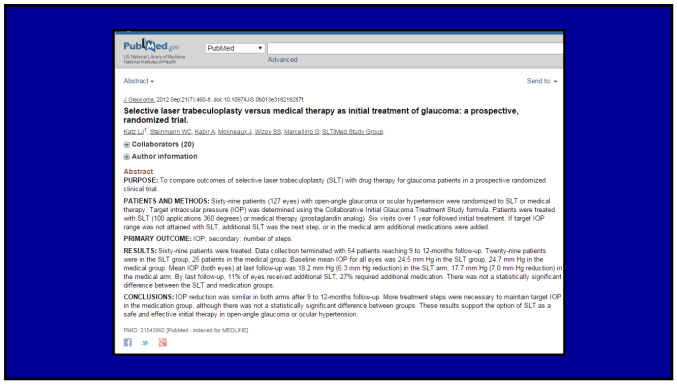

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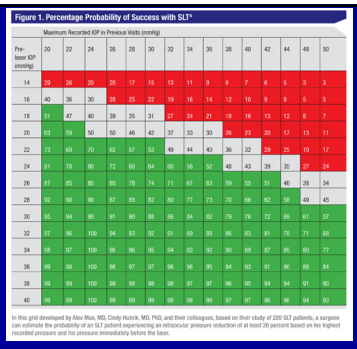
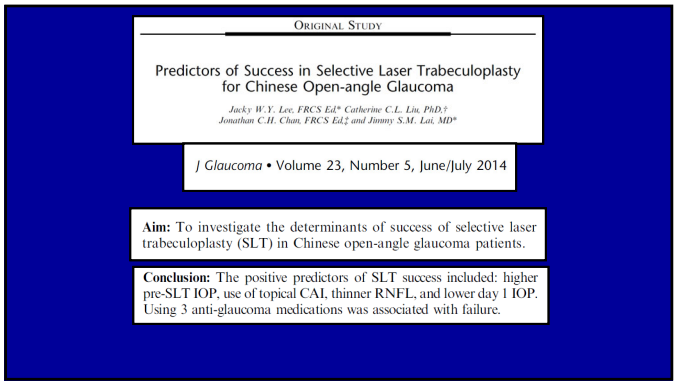


Mao, Hutnik, et al

82



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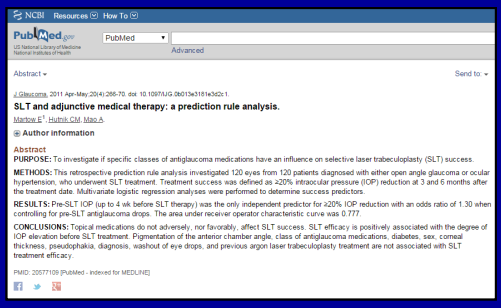

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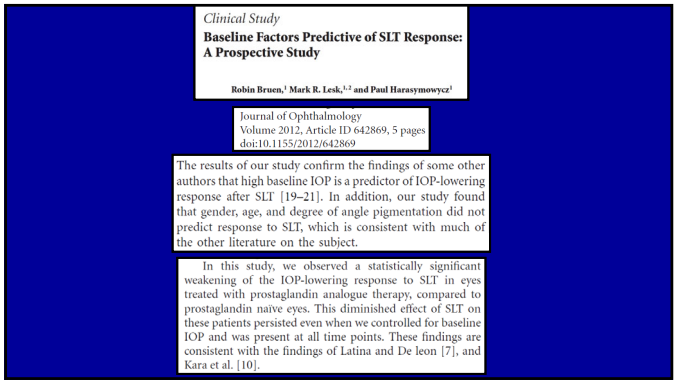

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- Newly diagnosed OAG and OHTN (treatment-naïve)
- Two groups:
  - Medicine 1st
  - Laser 1st
- Compared
  - HRQoL
  - Clinical Efficacy
  - Cost effectiveness
- Followed for 36 mo

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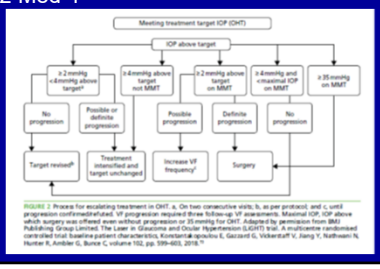
LiGHT Trial

- 356 SLT-1
- 362 Med-1



85

Is There Another Bag?

88

LiGHT Trial Results

- 91% patients completed 36 months
  - No difference in HRQoL
  - Proportion of patients at target IOP:
    - SLT-1 93% (0 patients requiring surgery)
    - Med-1 91% (11 patients requiring surgery)
  - SLT-1 provided medicine-free treatment for at least 36 months in 74% of group

86

Surgery Indications

- Progressive visual field loss or optic nerve/nerve fiber layer loss despite maximum tolerated medical therapy
- Problems with adherence, allergies, intolerance to medications

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SELECTIVE LASER TRABECULOPLASTY

- Consider when:
  - Non-compliance is an issue
  - There are undesirable or intolerable side effects from medications
  - Patient is on maximum tolerated medical therapy (?)
  - Surgical intervention is contraindicated

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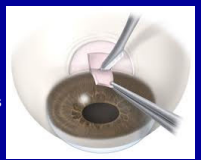
Trabeculectomy

- Goal: Create fistula between anterior chamber and subconjunctival space
- Success is dependent on surgery but also highly dependent on post-surgical care
- Advantages:
  - No devices ($$)
  - Can achieve very low IOP
- Disadvantages:
  - Complications up to 40% cases
  - Failure up to 50% at 5 years
  - Cataract formation



90

Filtration Surgery - Complications

- Early
  - Hyphema
  - Inflammation
  - Low IOP
  - IOP spike
    - Deep AC
    - Shallow AC
  - Endophthalmitis (rare in early post-op period)

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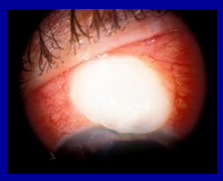
Filtration Surgery Complications

- Late Complications:
  - Bleb leak
  - Hypotony
  - Blebitis/Endophthalmitis
  - Scarring of ostomy



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Alternatives to Trabeculectomy: Ex-Press Mini Shunt

- Non-valved, MRI compatible stainless steel device with 50micron lumen
- Originally placed under the conjunctiva (complications), now placed under a scleral flap
- Lower incidence of hypotony compared to trabeculectomy
- Similar results with fewer early complications

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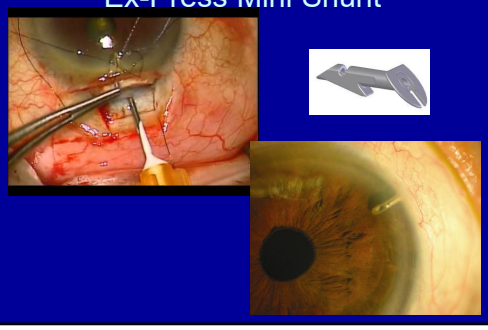
Ex-Press Mini Shunt



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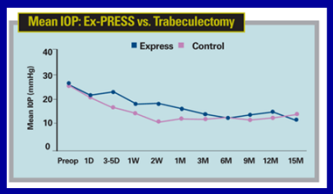
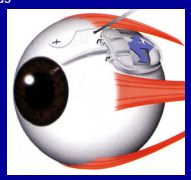


95

Alternatives to Trabeculectomy: Tube Shunts

- AKA Glaucoma Drainage Device
  - Historically used in patients with previous trabeculectomy failure or secondary glaucomas
  - Now more common as initial surgical choice
  - TVT study
    - Early post-op complications
      - Tube 21% Trab 37%
    - Late post-op complications:
      - Tube 34% Trab 36%
    - Reoperation for surgical complications:
      - Tube 22% Trab 18%



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Minimally Invasive Glaucoma Surgery (MIGS)

- Aim to lower IOP with a better safety profile than filtration surgery
- Often termed “blebless” surgery
- Generally rapid recovery (same as cataract surgery) with minimal impact on quality of life
- Typically indicated for mild/mod POAG

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Typical MIGS Features

- *Ab interno*
- micro incision
- Minimal trauma
- Efficacy
- High safety profile
- Rapid recovery

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MIGS – Ab Interno

- Usually performed under gonioscopic view, usually through side port incision
- Most commonly performed at the same time as cataract surgery
  - Trabectome OR KDB (TM unroofing with blade)
  - Trabecular microbypass stent (iStent)
  - Xen gel
  - Hydrus
  - Endocyclophotocoagulation (ECP)

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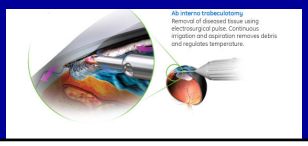
Trabectome

- Bipolar cautery on a handpiece inserted into the AC through the cataract incision
- Ablates and removes a portion of the TM to increase aqueous outflow
- Typical IOP goal is mid-teens
- Complications include hyphema, inflammation
- KDB (similar)



100

iStent

- Very small titanium device implanted through TM into Schlemm’s canal
- Goal is to improve aqueous outflow through conventional path (bypass TM directly into Schlemm’s canal
- FDA trials compared cataract surgery alone with cataract/iStent; at 12 months:
  - 68% cataract/iStent patients IOP </=21 without meds
  - 50% cataract surgery alone IOP </=21 without meds
- IOP not lowered as much as with trabeculectomy
- Fewer complications/less hypotony

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iStent

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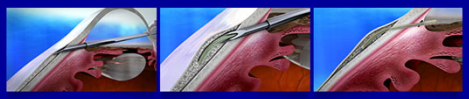
Xen Gel Stent (Allergan)

- Creates communication between anterior chamber and the subconjunctival space from the inside of the eye



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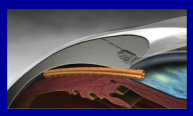
Other Stents

- CyPass Microstent (Alcon) - WITHDRAWN



- Hydrus Micro Stent (Ivantis)
  - Schlemm's Canal Scaffold

104

Other Procedures – Ab Externo

- Canaloplasty
  - Circumferential catheterization with suture tensioning of Schlemm's canal

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Endocyclophotocoagulation

- Endoscopic viewing system with laser, inserted through corneal incision and used to selectively ablate ciliary processes (decrease aqueous production)
- Mean decrease over 2 years = 7.1mmHg
- Not dependent on open angle/TM visualization

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How Do MIGS Compare to Trab?

- Few reports, somewhat difficult to compare
- Different complications
- Typically less IOP reduction with MIGS than with filtration
- Often seen as an intermediate step in glaucoma management
- Appeal: procedure at same time as cataract surgery

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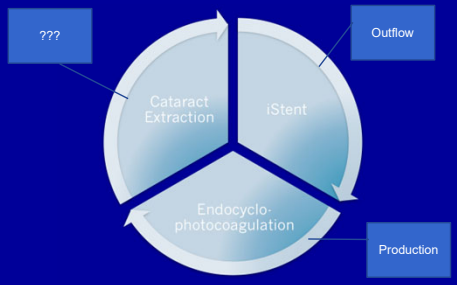
ICE Procedure



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MIGS – Final Point

- Since MIGS performed at time of cataract surgery, OD must be proactive in seeking surgeon who is experienced and willing to perform
- Don't miss the opportunity!

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Thank you for your attention!

DMarrelli@uh.edu

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