

## Managing Patients With Glaucoma

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### Premise Behind Managing Glaucoma

- What is the risk to our patient's visual function if we do nothing?
- If we accept that glaucoma has a natural history with a likely negative outcome, then we must intervene to alter the natural history and preserve vision

### Managing Glaucoma

❖ Managing glaucoma patients involves a series of decisions to be made over a lifetime of care

- ❖ Is disease present?
- ❖ Is therapy required?
- ❖ How severe is the condition?
- ❖ What should be the target IOP?
- ❖ How often should the patient be monitored?

### Who Do We Manage?

If damage exists at current IOP levels

Roughly, what is time difference between damage on rNFL and VF?

3 to 5 years

### Why the difference?

- Lots of overlap in visual system
- Significant damage must be done before functional changes are evident

Now what do we do?

Monitor closely?

Add additional medical therapy OS?

Do we treat OD?

## What Stage is this?

Table 3. AAO Glaucoma Severity Staging Descriptions.

STAGE	DESCRIPTION
Mild/early	Structural optic nerve changes consistent with glaucoma with no evidence of visual field changes with standard automated perimetry (perimetric glaucoma).
Moderate	Optic nerve changes consistent with glaucoma and glaucomatous visual field changes in one hemifield and not within five degrees of fixation.
Severe	Optic nerve changes consistent with glaucoma and glaucomatous visual field changes in both hemifields or loss within five degrees of fixation in at least one hemifield, or both.
Inferior/mature	Field not done, or patient unable to perform visual field testing.
Unspecified	Stage not recorded in chart.

No Cure

To stop progressive damage

Real Goal of Therapy

Table 1. Major Glaucoma Clinical Studies and Select Results

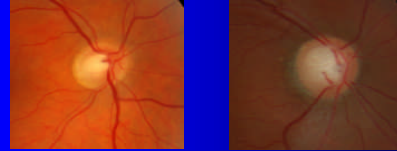
STUDY	SIGNIFICANT RESULTS
Ocular Hypertensive Treatment Study <sup>1</sup>	•Quantification of risk of conversion from ocular hypertension to glaucoma over a 5-year period. •Importance of central corneal thickness, IOP and vertical cup-to-disc ratio in assessing risk of conversion from ocular hypertension to POAG.
Early Manifest Glaucoma Trial <sup>2</sup>	•Lowering IOP reduces risk of glaucoma progression. •Visual field more sensitive than evaluation of disc changes in identifying progression.
Advanced Glaucoma Intervention Study <sup>3</sup>	•A treated IOP of less than 18mm Hg, at all visits, significantly reduces the statistical risk of progression.
Diurnal Fluctuations in IOP <sup>4</sup>	•Large diurnal fluctuations in IOP are an independent risk factor in POAG.
Collaborative Normal Tension Glaucoma Study <sup>5</sup>	•Minimal IOP may be lowered significantly (50%) to reduce risk of progression in normal tension glaucoma.
Los Angeles Latino Eye Study <sup>6</sup>	•Large vertical cup-to-disc ratio greater than 0.8 is strongly associated with risk of POAG in this ethnic group.

1. Katz M, Heuer D, Higginbotham E, et al. The ocular hypertensive treatment study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open angle glaucoma. Arch Ophthalmol 2002; 120: 1070-1078.  
2. Heijl A, Lunde C, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression. Arch Ophthalmol 2002; 120(10): 1268-75.  
3. Weinreb RN, Khaw P, Mansfield DC, et al. The advanced glaucoma intervention study (AGIS): The relationship between control of intraocular pressure and visual field deterioration. Am J Ophthalmol 2000; 130: 402-415.  
4. Johnson D, Johnson D, Johnson J, et al. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. J Glaucoma 2000; April; 9(2): 134-42.  
5. Collaborative Normal Tension Glaucoma Study. Cur Opin Ophthalmol 2003; April; 18(4): 287-95.  
6. Kim B, Weiss R. Glaucoma in Latinos/Hispanics. Cur Opin Ophthalmol 2010; March; 21(3): 198-5.

## Factors To Consider When Setting Target IOP

- IOP level at which ONH damage occurred

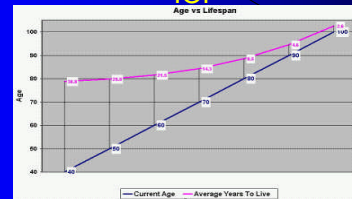
## Target IOP and Severity of Disease



## Consider the Rate of Progression of the Disease

- The faster the progression, the more aggressive you need to be

## Factors To Consider When Setting Target IOP



Patient Age or expected life span

## Factors To Consider When Setting Target IOP

- Corneal thickness
- Race
- Family history

## "Targets"

- 25% IOP reduction for OHTN or mild glaucoma
- 30% for moderate glaucoma
- 35% or more for severe glaucoma

## Common Mistake

- Patient is at or below target IOP and you mistakenly assume that the glaucoma is under control

## Detection of Progression Remains Subjective

## Perimetry and the Detection of Progression

- Elliot Werner had 6 MDs evaluate series of fields
  - task was to decide if progression had occurred
  - Dr. Werner knew which patients had gotten worse

## Perimetry and the Detection of Progression

- There was no clear cut consensus on many of them
- Only 5/6 MDs agreed on 15 of 30 patients

## How are patients non-compliant?

- They occasionally miss doses
- They don't take meds at all
- They take meds but don't come in for regular visits

## What percentage of glaucoma patients are noncompliant?

40 to 50%

## Your Patients Are Liars!!!

## What is #1 reason for noncompliance

Forgetfulness

## Reminder calls

- Apps
- Set their alarm clock

## Keep a Reasonable Schedule

Frequency of Dosing	Compliance with Dosing	Compliance with Timing
QD	79%	74%
BID	69%	58%
TID	65%	46%
QID	51%	40%

## Limit the # of Bottles

- Optimal Therapy different from Maximal Therapy
- Two bottle limit
  - Addition of third bottle rarely provides substantial IOP reduction

## What is #2 reason for noncompliance

Cost

### Pick a realistic medication for your patient

- Many patients can get a generic topical beta-blocker for \$4/month
- Most prostaglandins cost \$35/month

### Cost and Compliance

Class	Brand Name	Generic Available
Alpha 2 Agonist	Alphagan P	Yes
Beta Blocker	Timoptic	Yes
Carbonic Anhydrase Inhibitor	Trusopt	Yes
Prostaglandin	Xalatan/Travatan/ Lumigan	Yes
Combination	Cosopt	Yes
Combination	Combigan	No

### What is #3 reason for noncompliance

Poor understanding of the disease

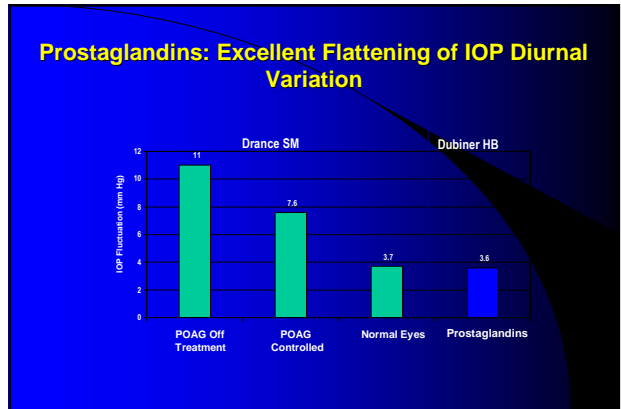
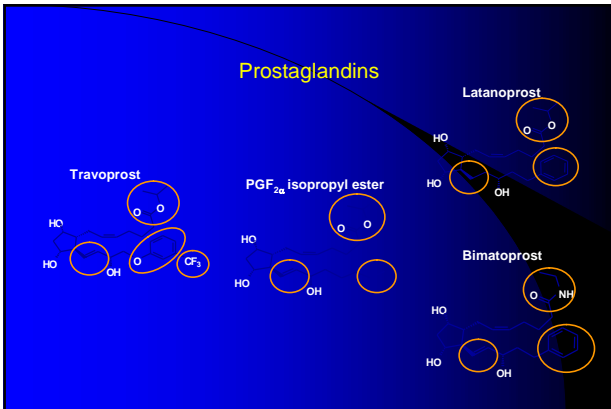
### Talking to Your Patients

- Involve patients in their care
- Assume everyone has a literacy problem
- Offer small amounts of info at a time
- Provide written materials at 5<sup>th</sup> grade reading level or below

### Limit the # of Refills

- “Forces” patients to come back to you intermittently
- Every patient visit should encourage patients to keep taking their medications

### Mechanism of Action of Prostaglandins



People Get Worse. . .

- Because we have no cure

People Get Worse. . .

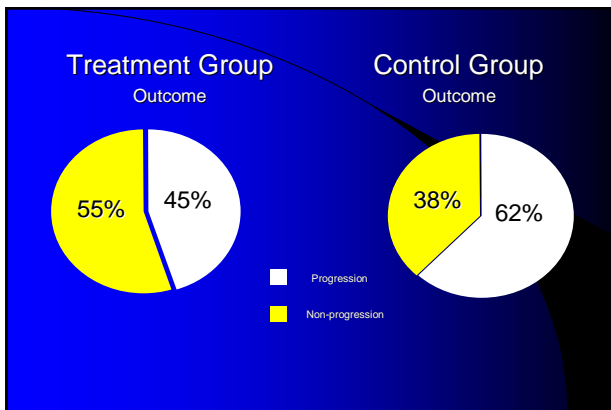
And because patients live longer

### How much should we lower IOP?

- Every point is important

### Early Manifest Glaucoma Trial

- 255 patients with glaucomatous visual field loss
- Randomized into treatment or observation group
  - Examination every 3 months
  - Stereo ONH photos every 6 months
  - 30-2 Full Threshold VF every 3 months
  - Follow-up for at least 4 years



For most patients with glaucoma . . .

The question is not IF they will get worse

The question is WHEN they will get worse

### Beta Blockers

- ➔ Beta blocker in AM, PG in PM
- ➔ Beta blockers have a proven record

### Beta Blockers

- Onset of Action 30 minutes
- Maximum effect 1-2 hours
- Peak efficacy after two weeks

### Contraindications to Beta-Blockers

- Congestive Heart Failure
- COPD
- Asthma
- Emphysema
- Athletes: Does not allow for heart rate to exceed 135 BPM

### Beta Blockers: Advantage

- ➔ Easy to follow schedule
- ➔ Generic beta blockers are relatively inexpensive
- ➔ Can generally get 1.5 to 2.0 mm hg additional IOP lowering



### Problem with Beta Blockers

- ⇒ No effect on diurnal variation
- ⇒ Does not help IOP at night

### Brimonidine

- ⇒ FDA approved for TID dosing
- ⇒ Most prescribe as BID dosing
- ⇒ Can get additional 2.5 mg Hg IOP lowering

### Brimonidine

- ⇒ No effect on diurnal variation
- ⇒ Does not help IOP at night

### CAIs as adjunctive therapy

- ⇒ Sulfa based drug
- ⇒ Most prescribe BID

### Topical CAI as adjunctive therapy

- Lowers IOP better than others
- Decreases nocturnal IOP
- Decreases diurnal variation

### Adjunctive Therapy



*Topical CAI May be best additive agent to prostaglandin*

## Combining the Prostaglandins

“The combination of bimatoprost and latanoprost in POAG increases the IOP and should not be considered as a therapeutic option.”

Doi LM et al. *Effects of the combination of bimatoprost and latanoprost on intraocular pressure in primary open angle glaucoma: a randomized clinical trial.* Br J Ophthalmol 2005;89(5):

## Combination Products

- Simbrinza – brinzolamide/brimonidine
- Combigan – brimonidine/timolol
- Cosopt – dorzolamide/timolol
- Rocklatan – Rhopressa with PG

## Advantage of Combination Products

- Adds another medication to medical regimen without adding another bottle

## Advantage of Combination Products

- Keeps costs down since only one copay

## Advantage of Combination Products

- Less preservatives since 2 drugs in one bottle

## Disadvantage of Combination Products

- Mismatch of dosing in many cases

## Disadvantage of Combination Products

- Combination products don't work as well together as they do individually

## Disadvantage of Combination Products

- Is third drug helping all that much?

## Combination Products: Did You Know ...

- All glaucoma medications have a non-response rate of roughly 10% so there is a 20% chance that one of the components of any combination drug is not doing anything

## Vyzulta

### Nitric Oxide and Glaucoma

Patients with primary open-angle glaucoma (POAG) have lower levels of NO synthase activity in the trabecular meshwork (TM), Schlemm's canal, and stony muscle and reduced NO metabolites in the aqueous humor.<sup>1,2</sup>

NO donors lower IOP in normal and POAG eyes.<sup>3,4</sup>

A major site of action for NO donors is the trabecular meshwork.<sup>5,6</sup>



## Problem with Rhopressa

- \$\$\$\$
- Hyperemia
- Use discount cards
- Hopefully price will come down soon

## Neptazane (Methazolamide)

- Usually dosed 50 mg BID
- Also Sulfa drug with similar side effects

## Memantine

- FDA approved to treat Alzheimer's
- Works on NMDA receptor to prevent an excess of glutamate
- Dosed anywhere from 5 mg a day to max of 28 mg a day

## My ideal plan for progressive glaucoma patients

- Switch them from PG to Vyzulta

## Rule # 1

- Find out why a patient's glaucoma is worse
  - i.e. is it due to noncompliance
- Really the only time I consider surgery

## Rule # 2

- If the patient is hypertensive, find out if they are on an oral beta blocker
- If so, no value in adding a beta blocker, which also means the combination beta blocker products

## If patient is hypertensive

- See if they can take their meds in AM instead of at bedtime
- Will help increase perfusion pressure at bedtime
- Will help lower IOP in AM

## Rule # 3

- If rule # 1 and #2 not violated, then perform serial tonometry to estimate when the patients IOP is the highest
- Realize that each medication you add follows the law of diminishing returns

### My preference for 2<sup>nd</sup> line therapy if IOP highest in AM

- Beta-blockers in AM
- Prostaglandins at night time

### My preference for 2<sup>nd</sup> line therapy if IOP highest other time of day

- Azopt or Simbrinza BID
- Prostaglandins at night time

### Who do I treat 100% of times

- Anyone with consistent, reliable, repeatable and/or progressive changes in ONH, rNFL, or VF

### Who do I treat 100% of times

- Anyone with an IOP of 28 or greater

### Who do I treat 100% of times

- Anyone with C/D .80 or above

### Who do I treat 100% of times

- Anyone who wants to be treated to decrease their risk of converting from glaucoma suspect to glaucoma