Alternatives for the progressing low tension patient: Non evidence based medicine

John R. Samples
My glaucoma “vitamin”

- Resveratrol 250 mg qd  Basis: Weinreb ARVO 2011
- Fish oil 3000 mg qd  Basis: Knepper and me at ARVO 2009
- CoQ10  Basis: European glaucoma meeting, Paris 2011
- Ascorbic acid  Basis: Common sense
- B12/Cyanocobalimine  Basis: Len Levin, Banff meeting Sept 2011
- Any vitamin that contains zinc

Several instances here

- Classic low tension (Levene: Never over 22)
- Patients progressing in the low teens who decline further surgery
- Unclear, muddy cases with glaucomatous looking nerve, severe myopia and family history
Other considerations

• A lot of low tension glaucoma is really failure to diagnosis high tension glaucoma where the pressure is higher at night, esp in individuals with sleep apnea, CPAP etc.

• Hypertension and Hypotension both play a role in glaucoma. Hypertension has been shown to damage RGC using psychophysical methods

Slide 3

• The best medication
  • Last a long time, is not heat inactivated, once a day or better, no BAK and, possible to monitor compliance, highly usable (Doesn’t drizzle out of the bottle)

• The best laser
  • No histologic side effects; can be repeated; does no harm (MDLT, SLT, Sapphire Titanium, but not ALT)

• The best surgery
  • Flattens the curve, doesn’t leave the patient infection prone, rarely has to be repeated, can be used in a third world setting (We aren’t there yet but much potential is found in the new glaucoma procedures)
Drugs for glaucoma

A. Traditional: IOP lowering
B. Neuroprotection: High interest, many candidates
C. Cytoprotectants
D. Laser trabeculoplasty enhancers
E. New surgery enhancers
F. Nutritional
G. Alternative
H. Treat the etiology (Antagonize sCD44 and/or dissolve Versican)
I. Gene Therapy (Also genetic profiling of which meds to use)

A. Traditional outflow enhancers
Future targets: Outflow

- Collector channels: Nonvalved capillary cells which contain actin in their vascular walls
- Juxtacannaclicular meshwork: Now accessible with I-Science and similar technologies
- Wall of Schlemn’s canal: Ditto
- None of these are likely to help with progression at low pressure

B. Neuroprotection

- Many under development borrow from the neurosurgery literature
- Variety of strategies
  - Most recognize the glial cell as a potential culprit in glaucoma
- One interesting development: Resuscitation of the discontinued unoprostone (Rescula) as a neuroprotectant
Drugs that have been used by glaucoma specialists in low pressure progression

- Calcium channel blockers (I use Procardia XL)
- Memantine
- Brimonidine
- Ginko (Variability in preparations)
- I have used at least ¾ in desperate situations

Drugs that have been avoided in low tension situations

- Beta blockers !!!
C. Cytoprotectants

- Corticosteroids
- Prostaglandins
- CBLI Drugs
- Many other classes

D. Laser Trabeculoplasty Enhancers

- Enhance IL1 and TNFalpha elevation after LT
ALT, SLT, MDLT, Saphire Ti

- Change the MMPs:TIMPs ratio via cytokines (Also any trauma and phaco!)
- ALT more likely to damage juxtacannalicular meshwork
- ALT more visible than SLT or MDLT
- SLT or MDLT more repeatable ???
- MDLT less expensive
- Saphire Ti may be superior; deep reach
What does the laser do?

- The cytokines TNF and IL-1 mediate the MMP-3 increase that occurs in response to trabecular meshwork (TM) treatment by laser trabeculoplasty

Mojgan Hosseini,1 Anastasia Y. Rose,1 Kaili Song,1 Cynthia Bohan,1 J. Preston Alexander,2 Mary J. Kelley,1 and Ted S. Acott1

*Investigative Ophthalmology and Visual Science.*
2006;47:1469-1476.)

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1From the Casey Eye Institute, Oregon Health & Science University, Portland, Oregon; and 2Triple Point Biologics, Forest Grove, Oregon.
E. “New surgery” Enhancers

- Access to suprachoroidal space
- Access to Schlemm’s canal
- Many medications that affect outflow may be more effective when placed “on site”

Results - Light Microscopy

At 7 mmHg, the aqueous plexus (AP) is more open compared to the tissue perfused at higher pressures. At 15 mmHg, there is focal herniation of the inner wall and JCT at the collector channel (CC) ostia. At 30 and 45 mmHg, more dramatic herniations of the inner wall and JCT into the collector channel ostia were found.

Furthermore, collapse of the AP with increasing pressure is not uniform. Collapse is more complete near the collector channel ostia.
F. Nutritional

- Zinc containing vitamin in all glaucoma patients
- Fish oil in all patients
- Maybe resveratrol if they want to go out on a limb but disclose the level of evidence to the patient
- Ascorbic acid (but not if going to filter)
G. Alternative

- Marijuana
- Alcohol

Marijuana

- 200 pharmacies on Broadway in Denver
- Approved specifically for glaucoma in Oregon
- Approve for just about anything in Colorado (No Rx required in two cities)
- Pressure efficacy only while “stoned”
- How to handle patients?
WONDER WINE ‘CLEANS BLOOD VESSELS'

An Australian doctor says he has created the world's healthiest wine, which cleans your blood vessels and reduces the risk of heart attack as you drink it.

Each bottle contained up to 100 times the amount of resveratrol - a naturally occurring anti-oxidant found in grapes - than a standard drop, says Sydney's Dr Philip Norrie.

December 15, 2008, Australian Associated Press

Another alternative

• Doctor in Gresham, OR, PhD in nutrition at MIT
• Claims glutathione tablets made into tears lower IOP (and reverse some cataract changes)
• Evaluations to date, same time of day but not masked, has removed glaucoma meds in numerous patients
• Controlled, masked trial suggested…….
H. Treat the Etiology

- sCD44
  - Damages TM and RGC
  - Always elevated in high pressure glaucoma
  - Over-expression always increases IOP
- Versican
  - Associated with low flow of meshwork
  - Specific relationships with sCD44

Neuro-degenerative Diseases

- Disease
  - Alzheimer’s
  - Parkinson’s
  - Amyotrophic lateral sclerosis
  - SCA
  - POAG

- Protein
  - B-amyloid
  - α-synuclein
  - Superoxide mutase
  - Ataxin
  - sCD44

* Mitochondrial dysfunction and + altered phosphorylation
Although it is almost hopeless boring, the next slide is what really causes open angle glaucoma........

Versican
Immunostaining of versican: strong in JCT and near cells and beams and also around a blood vessel in sclera (Acott, Keller, Kelley, Samples 5/19/2009)

I. Glaucoma Genes

- Gene Therapy is possible
- Vector/Delivery systems are improving
- Genetic profiling of patients who will respond to specific drugs
Primary Open Angle Glaucoma:
All are AD

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Glaucoma Therapy

- Alternative therapies when progressing at low pressures should be completely discussed
- Med selection based on genetic profile (See June 26 web page on Newsweek.com)
- Neuroprotectants
- Better laser therapy: Not a good low tension choice
  - Medical enhancement
  - Better frequency
- Surgical improvements: Lower IOP with no bleb
What’s the next drug you are going to see for glaucoma?

- Rho Kinase Inhibitor
- Azopt-brimonidine
- PGE 3 and PGE 4 drugs
- Anecortave acetate
- PGF internal depot drug
- I personally would like to see a glaucoma vitamin even though the science is skimpy

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