A Unique Presentation of Steroid-Response Glaucoma

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Disclosures

- The Presenter and Organizers for “A Unique Presentation of Steroid-Response Glaucoma” by Dr. Carissa Hintz have no financial relationship with any company or products mentioned in this presentation.

Case History

- 52 year old female referred for glaucoma evaluation
- Referring doctor noted IOPs of OD 56 and OS 53 by GAT
- Chief Complaint: referred for high IOP, blurred vision OD>OS, glare and difficulty with night driving that was progressing, no pain is noted
- (+)FHx glaucoma: Father
- Medications: Lipitor, Imitrex, Nexium, Singulair, natural progesterone/testosterone, lotemax 3x per week, Nasacort QD, steroidal rescue inhaler pm, lumify
- PH reports ocular health unremarkable besides myopia.

Pertinent Exam Findings

- Pupils: PERRLA (-) APD OD/OS
- ETOMs: Full, no restrictions OD
- IOP by GAT: OD 66 OS 60
- Gonioscopy: Open to CB 360, (-) PAS, flat iris approach
- Pachymetry:
  - OD: 495 microns
  - OS: 497 microns

Ocular Health Findings

- Anterior Segment:
  - OD: trace NS, 1+ cortical, 1+ PSC, deep & quiet anterior chamber (-) cells
  - OS: trace NS, 1+ cortical, trace PSC, deep & quiet anterior chamber (-) cells
- Posterior Segment:
  - OD: glaucomatous cupping (0.85/0.85), otherwise unremarkable
  - OS: glaucomatous cupping (0.75/0.75), otherwise unremarkable
Differential Diagnoses

- Angle Closure
- Glaucomatocyclitic Crisis
- Open-Angle Steroid Response Glaucoma

Treatment and Follow-Up

- Initial treatment included Diamox, Simbrinza, Timolol, Travatan Z and Rhopressa.
- Lotemax and Nasacort were D/C.
- 2 days later: IOP 10 OU
  - D/C Rhopressa
- 1 week: IOP 14 OD 13 OS
  - acetazolamide and Timolol were D/C due to adverse effects.
Long-term Treatment

- In chronic steroid-induced glaucoma, normalization of IOP following D/C of steroids usually takes 1-4 weeks.
- 2 weeks: IOP 18 OD and 16 OS
  - Discuss treatment options: pt chose to pursue SLT
- 1 day post-op SLT OD:
  - IOPs were 18 OD with Simbrinza TID OD and Travatan Z QHS OD.
- 1 day post-op SLT OS:
  - IOP 18 OD and 14 OS.
- 2 months post-op SLT:
  - IOP 14 OU

Mechanism

- Steroid response glaucoma results in elevated IOP thought to be secondary to increased outflow resistance. Thoughts on what causes this include:
  - Upregulation of glucocorticoid receptor on TM cells.
  - Glucocorticoids increase expression of fibronectin, glycosaminoglycans, and elastin.
  - May suppress phagocytic activity leading to increased deposition in the juxtacanalicular meshwork.
  - Glucocorticoid also decreases the synthesis of prostaglandin, which regulates aqueous outflow.

Epidemiology

- Most studies have focused on adults, but children have been known to have significant steroid response to nasal sprays.
- Risk factors for being a steroid responder include:
  - POAG patients (20% of glaucoma suspects and 90% of POAG might have an ocular hypertensive response to 4 week dose of dexamethasone)
  - First degree relatives of POAG patients
  - High myopia or history of refractive surgery or corneal transplant
  - Very young and older patients (bimodal distribution)
  - Diabetes Mellitus or connective tissue diseases like Rheumatoid Arthritis
  - Eyes with pigment dispersion syndrome or traumatic angle recession

Response Categories

- High steroid-responders: 4.6%
  - IOP >31mmHg
  - Increase of >15mmHg from baseline
- Moderate steroid-responders: ~1/3
  - 20-31mmHg
  - Increase of 6-15mmHg
- Mild steroid-responders:
  - <20mmHg
  - Increase of ≤15mmHg

Table 2: Steroid response by risk factor

<table>
<thead>
<tr>
<th>Steroid Response by Risk Factor</th>
<th>Population</th>
<th>Normalization</th>
<th>Hypertensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>POAG patients</td>
<td>30-40</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Non-POAG patients</td>
<td>10-20</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Overall (IFCIC)</td>
<td>15-20</td>
<td>15</td>
<td>15</td>
</tr>
</tbody>
</table>

Timeframe

- Steroid response usually occurs 3-6 weeks following steroid use; however, it can occur earlier.
- It can take several months for corticosteroid injections to cause a steroid response.
Which Steroids are the Worst?

- All forms of steroids can cause an IOP spike; however, the most at risk forms are topical (drops or ointment applied directly to the eyes or eyelid skin), intravitreal, periocular, and nasal sprays.
- The pressure-inducing effect is directly proportional to the anti-inflammatory potency and to the dosage used.
- Intranasal steroids come in 2 generations:
  - 1st generation: budesonide, beclomethasone dipropionate, and triamcinolone acetonide. Higher systemic bioavailability compared to 2nd generation (up to 49%). High risk of steroid-response.
  - 2nd generation: mometasone furoate, fluticasone propionate, and fluticasone furoate. Systemic bioavailability is <1%.

Types of Intranasal Steroids

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Common Brands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide</td>
<td>Entocort, Uceris, Pulmicort</td>
</tr>
<tr>
<td>Beclomethasone dipropionate</td>
<td>Qvar</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Nasacort</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Nasonex</td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>Flonase</td>
</tr>
<tr>
<td>Fluticasone furoate</td>
<td>Veramyst</td>
</tr>
</tbody>
</table>

Treatment Options

- Discontinuation of steroids.
  - May need to substitute with non-steroidal option if anti-inflammatory is needed.
  - Medical therapy should be initiated.
  - If medical therapy is insufficient, SLT should be considered followed by glaucoma surgery if necessary.
  - MIGS can also be considered if cataracts are visually significant to indicate cataract extraction.
- SLT appears to be effective for these patients according to multiple case reports and studies.

Medical Therapy

<table>
<thead>
<tr>
<th>Class</th>
<th>Mechanism</th>
<th>Average IOP Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostaglandin Analogues</td>
<td>Increase uveoscleral outflow</td>
<td>20-35%</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>Decrease aqueous production</td>
<td>20-25%</td>
</tr>
<tr>
<td>Alpha-2 Agonists</td>
<td>Reduce aqueous production and increase uveoscleral outflow</td>
<td>20-25%</td>
</tr>
<tr>
<td>Carbonic Anhydrase Inhibitors</td>
<td>Reduce aqueous production</td>
<td>22%</td>
</tr>
</tbody>
</table>

New Medications

- Latanoprostene bunod (Vyzulta)
- Netarsudil (Rhopressa)
- Netarsudil/latanoprost (Rocklatan)
Latanoprostene bunod

- Vyzulta (latanoprostene bunod)
  - Cleaves into latanoprost acid and nitrile oxide-donating moiety
  - NO donors relax the TM and increase aqueous outflow
  - Significantly greater IOP reduction compared to latanoprost
  - 32% reduction in IOP

Netarsudil

- Rhopressa (netarsudil)
  - IOP reduction mechanisms:
    - Increased outflow through conventional pathway
    - Decreased episcleral venous pressure
    - Decreased aqueous production
  - Latanoprost > Rhopressa > timolol
  - 15-22% IOP reduction

Netarsudil/latanoprost

- Rocklatan (netarsudil/latanoprost)
  - Superior to netarsudil and latanoprost alone
  - Targets both the conventional and uveoscleral outflow
  - 60% of patients achieve an IOP reduction of 30% or more
  - Nearly twice that of latanoprost alone

Surgical Options

- SLT: Pigmented cells in the TM are targeted by a laser effectively destroying these cells and causing a signal for macrophages to increase activity at the site of the TM. This increases TM outflow.
  - Can take up to 6 months for full IOP lowering effect to be reached.
- Trabectome: Ablates the TM and decreases outflow resistance by opening a direct pathway into Schlemm’s canal.
  - Trabectome provides a safe and effective method to immediately lower IOP.
- Trabeculectomy or tube shunts may be considered if other methods do not adequately lower IOP.

SLT Efficacy

- Maleki et al. reported 46.7% success rate in steroid-induced glaucoma (IOP <22 mmHg and/or >20% IOP reduction). At 12 months there was a 30.4% average IOP reduction.
- Xu et al. reported 61.7% success rate in POAG at 1 year (IOP <21 mmHg with >20% IOP decrease or IOP <21 mmHg with decrease in meds).
- Potential to reduce dependence on medications and to repeat treatment.
Follow-up Care of SLT

- Complications:
  - Post-operative IOP spike
  - Usually within hours of the procedure
  - Exfoliation glaucoma patients – higher risk of long-term IOP increase
  - Iritis
  - Rarely hyphema, macular edema, and corneal haze

SALT Trial

- Studied impact of post-operative anti-inflammatories on efficacy of SLT
- 3 groups: NSAID, steroids, or placebo saline tears
- NSAIDs and steroids following SLT resulted in significantly lower IOPs than placebo saline tears
- Baseline IOPs were not statistically different

Mechanism of SLT Theories

- Mechanical theory:
  - Thermal energy burns the tissues
  - Collagen shrinks and contracts
  - Uveoscleral meshwork and Schlemm’s canal are stretched open

- Cellular and molecular biologic theory:
  - Laser energy stimulates cellular remodeling
  - Production of enzymatic metalloproteinases
  - Inflammation thought to play a role in TM remodeling
  - Inflammation can increase macrophage activity but may also elicit scarring/fibrosis

SALT Conclusions

- Medication in the first 5 days following SLT takes weeks to have an effect on IOP
- NSAIDS and steroids were thought to decrease scarring and fibrosis leading to greater IOP reduction
- Surgeons were allowed to choose how many degrees to treat
- Smaller studies have found no difference in efficacy between steroids and placebo

Conclusion

- Performing a thorough case history is vital especially since many patients forget to mention OTC nasal sprays when asked about medications.
- Early detection is key as vision loss can occur rapidly if medical management is not initiated to reduce significantly elevated IOPs.
- SLT is efficacious for steroid-responsive glaucoma
- New studies are showing that NSAIDS following SLT may increase IOP-lowering efficacy.
References


