New perspective in glaucoma treatment

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No financial interest

What is glaucoma?

Glaucoma treatment

***IOP***
Something to work on “Drug”

- Toxic from preservative
- Poor adherence
- Better choices

Trend of medical treatment

- Avoid preservative
- Combination drops
- New drug delivery system
- Novel mechanism of action

Percent of preservative

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Active Ingredient</th>
<th>Trade Name</th>
<th>Preservative</th>
<th>Contact Lens Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine 0.02%</td>
<td>Lunugan</td>
<td>BAK 0.001%</td>
<td>15 minutes</td>
<td>Yes</td>
</tr>
<tr>
<td>Timolol 0.5%</td>
<td>Timoptic</td>
<td>BAK 0.001%</td>
<td>15 minutes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dorzolamide 2%</td>
<td>Carteol</td>
<td>BAK 0.001%</td>
<td>15 minutes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ofloxacin 0.3%</td>
<td>Ofloxin</td>
<td>BAK 0.001%</td>
<td>15 minutes</td>
<td>Yes</td>
</tr>
<tr>
<td>Brinzolamide 1%</td>
<td>Brintal</td>
<td>BAK 0.001%</td>
<td>15 minutes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Carteol, Arteoptic BAK 0.005%

Combination drops

<table>
<thead>
<tr>
<th>Brand Name (Mfg.)</th>
<th>Generic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbimol (Allergan)</td>
<td>timolol 0.5%, brimonidine 0.2%</td>
</tr>
<tr>
<td>Concept/Concept PF (Alcon)</td>
<td>timolol 0.5%, dorzolamide 2%</td>
</tr>
<tr>
<td>Rozman (Alimta)</td>
<td>nefimox 0.2%, latanoprost 0.005%</td>
</tr>
<tr>
<td>Sermbrin (Alcon)</td>
<td>brimonidine 1%, brinzolamide 0.2%</td>
</tr>
</tbody>
</table>

Available in US
Available outside US
Xalcom (Pfizer) latanoprost, timolol
Ganfort (Allergan) bimatoprost, timolol
Duo-Trav (Novartis) travoprost, timolol
Azarga (Novartis) brimonidine, timolol
Preservative free

New drug delivery system

• 45% of patients used their once daily drops less than 75% of the time


COMOD system

New drug delivery system

Sustained-Release Drug Delivery: Closer Than You Think!

By Devesh K. Varma, MD, FRCSC
Gel forming drop

- **Solidrop**
  - Preclinical study with brimonidine
  - Retention up to 28 days
  - No preservative, no irritation
  - No IOP reduction in control eye

Surface implants

- **TODDD (Topical ophthalmic drug delivery device)**
  - Load with polymer drug
  - Preclinical study: Timolol (180 days)

- **Brimonidine Ring**
  - Phase 2 clinical trial
  - 130 patients
  - Not inferior to timolol for 6 months

Punctal plug

- **OTX-TP (travoprost)**
  - Phase 2 clinical trial
  - Sustained release for 90 days
  - Small but easy to be identified (fluorescein)
  - No irritation but patient might not aware if it becomes dislodge

Novel mechanism of action

- New PGs
- Rock inhibitor
- Adenosine receptor agonist

Latanoprostene bunod

- K-115 (Ripasudil)
  - Glanatek: PMDA approved
- AR-13324 (Netarsudil)
  - Increase outflow (TM) + reduce inflow
  - Rhopressar (FDA approved)
  - Rhoclatan (Netarsudil+latanoprost: FDA approved)
- AMA0076
  - Reduce hyperemia

Rho kinase inhibitor

What’s new in Laser

- Selective laser trabeculoplasty (SLT)
  - Initial treatment option for open angle glaucoma
- Transscleral cyclophotocoagulation (TCP) and
  Endoscopic cyclophotocoagulation (ECP)
  - Need modification to improve safety profile

Electron microscope after laser

ALT  SLT

Alternative to SLT

**Table 3. Comparison of typical laser trabeculoplasty parameters**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Laser</th>
<th>Spot size (μm)</th>
<th>Duration</th>
<th>Power/energy</th>
<th>Number of spots</th>
<th>Degrees</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>Argon, blue/green 488/514 nm</td>
<td>50</td>
<td>0.1</td>
<td>300–500 μJ</td>
<td>50–100</td>
<td>180</td>
</tr>
<tr>
<td>SLT</td>
<td>Neodymium: yttrium aluminium garnet (Nd:YAG)</td>
<td>400</td>
<td>3</td>
<td>20–1 200 μJ</td>
<td>50–100</td>
<td>180–300</td>
</tr>
<tr>
<td>Nd:YAG</td>
<td>Diode, 810 nm</td>
<td>200</td>
<td>0.2 s (100 Hz)</td>
<td>1–2 W</td>
<td>50–100</td>
<td>180–300</td>
</tr>
<tr>
<td>Nd:V:YAG</td>
<td>Neodymium: vanadate (Nd:V:YAG)</td>
<td>300</td>
<td>7</td>
<td>50–100 μJ</td>
<td>50</td>
<td>180</td>
</tr>
</tbody>
</table>


The effect of cyclodiode laser in summary

<table>
<thead>
<tr>
<th>Clinical point</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient who could avoid further glaucoma surgery in the first year with single diode</td>
<td>21 (35.4%)</td>
</tr>
<tr>
<td>Patient who could avoid further glaucoma surgery in the first year with multiple diode</td>
<td>19 (32.2%)</td>
</tr>
<tr>
<td>Temporary effect (IOP decrease for 6–12 months)</td>
<td>11 (18.6%)</td>
</tr>
<tr>
<td>No effect (IOP before 6 months)</td>
<td>8 (13.4%)</td>
</tr>
</tbody>
</table>

**Laser cyclodiode as first surgical approach**
in patients with secondary childhood glaucoma and late-presented primary congenital glaucoma under the age of eight.

1. Research fellow at Moorfields Eye Hospital.
2. Clinical and Research fellow at Moorfields Eye Hospital and Great Ormond Street Hospital for Children.
3. Department of Ophthalmology, University Hospital, Autonomous University of Nuevo Leon, Mexico.
4. Honorary Research Fellow at Great Ormond Street Hospital and Foundation Doctor at Hinchingbrooke Hospital.
5. Ophthalmic Surgeon at Moorfields Eye Hospital and Great Ormond Street Hospital for Children.

S Petchyim, J Mohamed-Noriega, A Sharara, J Brookes.
What's new in glaucoma surgery?

MIGS (minimally invasive glaucoma surgery)

- Increase trabecular outflow
  - Trabectome
  - iStent
  - Hydrus stent
  - Excimer laser trabeculostomy
- Suprachoroidal shunt
  - Cypass microstent
- Sunconjunctival filtration
  - XEN gel stent

**MIGS**

- Indication
  - Mild to moderate glaucoma
  - Patients with cataract as the surgery may be performed simultaneously
Trabectome

Excimer laser trabeculostomy

- 308 nm excimer laser via fiberoptic
- Accurate tissue removal without inflammation (fibroblast found in outer wall of Schlemm's canal)

Pro:
- No implant
- Blebless

Cons:
- Lack of image guidance

iStent inject

Hydrus stent

“Intracanalicular scaffold”
Gonioscopy Assisted Transluminal Trabeculotomy (GATT)

- More IOP reduction
- Can be used in more advanced cases

XEN gel implant

- Controlled cyclodialysis
- 5 years RCT: Dramatic rise in corneal endothelial cell loss
Supramid

• ABC study
  ▫ Baerveldt produced greater IOP reduction
  ▫ Baerveldt had higher complication: hypotony

Stem cell therapy for glaucoma

• Early stage
  ▫ Trabecular cell
  ▫ Cell that provide "neuroprotective" effect

• Late stage
  ▫ Retinal ganglion cell

• Where are we now?
  ▫ Turn stem cell to "neuron"
  ▫ Transplant retinal ganglion into retina (Preclinical model)

Conclusion

• Trend of glaucoma treatment
  ▫ Drug
    ▪ Less or non preservative
    ▪ Physician dependent dosing
  ▫ Laser
    ▪ Primary or earlier intervention
  ▫ Surgery
    ▪ More options
  ▫ Stem cell therapy