This overview of Dorzolamide 2% eye drops was presented by Dr. Ravin N. Das, at Hotel Satya Ashoka, on 19-6-2004 in place of Dr. H. S. Ray due to unforeseen circumstances. This dinner meeting was sponsored by Cipla.

Dorzolamide
1. A topical Carbonic anhydrase inhibitor.
2. Ampholytic characteristics, hence good corneal penetration (depot effect achieved in cornea).
3. Achieves peak concentration 2 hours post dose.

Dorzolamide: Mechanism of action
1. Inhibition of Carbonic anhydrase II (in the ciliary process)
2. Slows down HCO$_3^-$ (bicarbonate) production
3. Reduction in sodium and fluid transport
4. Reduction in aqueous humor secretion
5. Lowering of IOP

Dorzolamide Clinical Efficacy Studies

Dorzolamide: Indian Study
(Cipla, Data on file)

Aim
Evaluation of safety and efficacy of 2% Dorzolamide eye drops as monotherapy or as an adjunctive therapy to beta-blockers in the treatment of POAG or ocular hypertension.

Design:
Open, prospective multi-centric study

Study conducted at
4 centers across the country
- Shri Ganpati Netralaya (Jalna)
- Guru Nanak Eye Center (New Delhi)
- St. John’s Eye Hospital and Medical College (Bangalore)
- Vittala International Eye Hospital (Bangalore)

Dorzolamide: Indian Study
(Cipla, Data on file)

Methods –
N=50 (79) eyes, M= 28, F=22
POAG: n = 38
OHT: n = 12, Treatment duration = 1 month
Follow-up visits at week 1, week 2 and week 4

IOP measurements: 8:00 am (trough drug levels) and 10:00 am (peak drug levels) (2 hours post dose)

<table>
<thead>
<tr>
<th></th>
<th>Monotherapy</th>
<th>Adjunctive Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of eyes</td>
<td>63</td>
<td>16</td>
</tr>
<tr>
<td>Baseline IOP (mm Hg)</td>
<td>23.24</td>
<td>22.43</td>
</tr>
</tbody>
</table>

Dorzolamide: Monotherapy
(Cipla, data on file)

- Overall, the percent reduction of the IOP from the baseline at the end of treatment period was
- 9.81% at trough drug levels
- 20.80% at peak drug levels

Conclusion
Dorzolamide is effective as monotherapy in POAG and OHT patients.
Results

- Overall, the percent reduction of the IOP from the baseline at the end of treatment period was
- 11.71% at trough drug levels
- 27.25% at peak drug levels

Conclusion

Dorzolamide is effective as adjunctive therapy in POAG and OHT patients.

Table: Incidence of adverse events by both monotherapy and adjunctive therapy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Monotherapy (n=63)</th>
<th>Adjunctive Therapy (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular stinging</td>
<td>38</td>
<td>4</td>
</tr>
<tr>
<td>Ocular burning</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Conjunctival hyperaemia</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Tearing</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dryness of mouth</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Allergic reactions</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

There were no significant cardiovascular changes at the end of 4 weeks

No serious adverse effects were noted

None of the adverse effects encountered above lead to the discontinuation of therapy.

Conclusion

Dorzox (dorzolamide 2%) is effective and well tolerated both as monotherapy and adjunctive therapy in the treatment of open angle glaucoma and ocular hypertension in INDIAN patients.

Dorzolamide: Comparison with timolol & betaxolol: One year study

Aim

To investigate the safety profile and efficacy of 2.0% dorzolamide (three times a day) for one year, compared with 0.5% timolol and 0.5% betaxolol (twice daily).

Design

A double-masked, randomized, parallel, multinational study

Setting

34 international sites

N = 523 (IOP > 23 mm Hg)

Follow up visits:

- Weeks 2 & 4 and Months 2, 3, 6, 9 & 12
- Ophthalmic examinations:
  - 2, 5 & 8 hrs post morning dose (7:30am)

Comparison of IOP reduction at peak drug levels at the end of 1 year.

Dorzolamide 2%, 3 times a day had comparable ocular hypotensive effect as compared to timolol 0.5% or betaxolol 0.5% administered twice a day.
Dorzolamide has ocular hypotensive efficacy comparable to beta blockers.
Dorzolamide was safe and well-tolerated.

Dorzolamide: Adjunctive Therapy (To latanoprost)

<table>
<thead>
<tr>
<th>Medication</th>
<th>No. of eyes</th>
<th>Mean baseline IOP (mm Hg)</th>
<th>Mean IOP at one year (mm Hg)</th>
<th>Mean IOP change (mm Hg [%])</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorzolamide ALL</td>
<td>25</td>
<td>19.8</td>
<td>16.0</td>
<td>-3.9 (19.7)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Dorzolamide BID</td>
<td>11</td>
<td>20.5</td>
<td>16.6</td>
<td>-3.9 (19.4)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Dorzolamide TID</td>
<td>14</td>
<td>19.4</td>
<td>15.5</td>
<td>-3.9 (19.9)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>23</td>
<td>19.9</td>
<td>17.4</td>
<td>-2.5 (12.3)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Brimonidine</td>
<td>25</td>
<td>21.0</td>
<td>19.0</td>
<td>-2.0 (9.3)</td>
<td>P = 0.0011</td>
</tr>
</tbody>
</table>

Conclusion

Dorzolamide is an effective adjunct to latanoprost and may be used effectively in glaucoma patients who require further IOP reduction.

Dorzolamide: Adjunctive Therapy To Timolol

Aim: To evaluate the efficacy of dorzolamide 2% in combination with timolol 0.5% in POAG or OHT patients.

Method

Large 1 year, parallel group, double masked, randomized, multinational study.

N = 23

Baseline & subsequent IOP readings taken 2, 5, 8 hours post morning dose (7.30 am)

Visits scheduled at weeks 2, 4, and months 2, 3, 6, 9, 12.

Results:

Overall % reductions of 29.2 and 27.3 at peak and trough drug levels respectively.

Concomitant therapy with dorzolamide 2% b.i.d and timolol 0.5% b.i.d has an additive effect on IOP in patients with POAG or OHT.

Dorzolamide: Vasoprotective effects

Dorzolamide: Vasoprotection

Aim: To evaluate effect of dorzolamide on ocular hemodynamics & visual function in POAG patients.

Method

Controlled, unmasked trial

N = 31 (2% dorzolamide topical T.I.D)

Duration: 9 months

Results:

- Patients visual fields significantly improved from MD -11.71 to -8.06 dB (p < 0.05)
- Optic nerve head blood flow increased from 508 AU at baseline to 644 AU
- Pulsatile ocular blood flow improved from 542 to 676 m/min (p < 0.05)

Conclusion

Dorzolamide has a significant effect on visual fields and pOBF in POAG patients and may significantly improve visual function.

www.mednet.ca/html

Dorzolamide: Vasoprotection

Aim: To study effect of Dorzolamide on visual function and ocular haemodynamics in NTG patients

Conclusion
**Dorzolamide 2% t.i.d.**

significantly reduced retinal AVP time and improved contrast sensitivity in NTG patients

May benefit NTG patients

**Dorzolamide: Vasoprotection**

**Aim**

To investigate and compare the microcirculatory effects of timolol, dorzolamide and latanoprost in newly diagnosed open angle glaucoma patients.

**Method**

N = 14

Baseline examination included IOP measurement and scanning laser ophthalmoscope angiograms (SLO)

3 groups = Dorzolamide 2%, timolol 0.5% or latanoprost 0.005%

**Duration of treatment**

4 weeks

AVP (arteriovenous passage times) times were assessed from SLO angiograms. (normal value = 1.45 secs)

**Conclusion**

Dorzolamide significantly shortened AVP times in newly diagnosed POAG patients as compared to latanoprost or timolol.

Dorzolamide treatment may benefit optic nerve head preservation by increasing ocular perfusion.

**Dorzolamide: Vasoprotection: Highlights**

- Accelerates blood velocity in the optic nerve head
- Benefits optic nerve head preservation
- Significantly shortens AVP times as compared to timolol and latanoprost
- Significant effect on visual fields and ocular blood flow in POAG patients
- Significantly improves contrast sensitivity in NTG patients.
- Benefits patients with retinal or optic nerve head vascular insufficiency

**Dorzolamide: Co-regulation**

\[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{HCO}_3^- + \text{H}^+ \]

Since dorzolamide blocks the transformation of CO2 to bicarbonate, it produces dual effect; increased CO2 in the eye improves ocular blood flow and less bicarbonate in the eye leads to reduced aqueous humor production, thus lowering IOP.

**Dorzolamide: Allied use**

- Prevention of IOP spikes
  - Post Phacoemulsification
  - Post laser surgery

Dorzolamide is safe and effective as apraclonidine in preventing IOP spikes after Nd: YAG laser surgery

**Dorzolamide: Safety and Tolerability**

- Well tolerated
- Not contraindicated in cardiac patients
- Does not cause metabolic acidosis or electrolyte imbalance characteristic of oral CAIs.
- No change in laboratory parameters (blood chemistry, CBC, urinalysis, BP and heart rate)
- Serious side effects like Stevens Johnson Syndrome, toxic epidermal necrolysis, aplastic anemia not reported to date.
- Safe and effective when used in combination with other topical medications
- Not associated with clinically meaningful changes of the cornea (no changes in corneal endothelial cell count)

**Dorzolamide: Indications, Dosage and Administration**

- Open angle glaucoma
- Ocular hypertension

If dorzolamide is used as a monotherapy, the dose is one drop in the affected eye(s) three times daily.

When used as an adjunctive therapy with an ophthalmic beta blocker, the dose is one drop in the affected eye(s) two times daily.

(If more than one topical ophthalmic drug is being used, the drugs should be administered at least ten minutes apart).

**DORZOLAMIDE: Highlights**

- First U.S. FDA approved topical CAI
- As monotherapy, reduces IOP by 18-26%
- Comparable efficacy to b blockers & brimonidine
- As an adjunctive therapy brings about additional 13-21% lowering of IOP
- Additive to multiple topical anti-glaucoma agents
- Good adjunct to latanoprost as compared to b blockers & brimonidine
- Does not produce acid-base or electrolyte disturbances & severe systemic adverse events associated with oral CAIs
- Provides “Vasoprotection”