

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

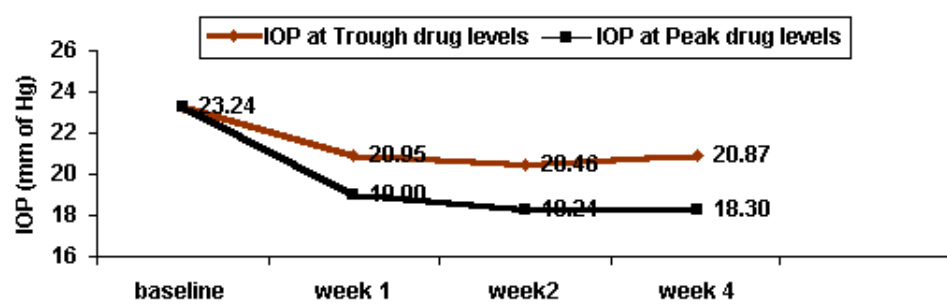
POAG: n = 38

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)

	Monotherapy	Adjunctive Therapy
No. of eyes	63	16
Baseline IOP (mm Hg)	23.24	22.43



Dorzolamide:

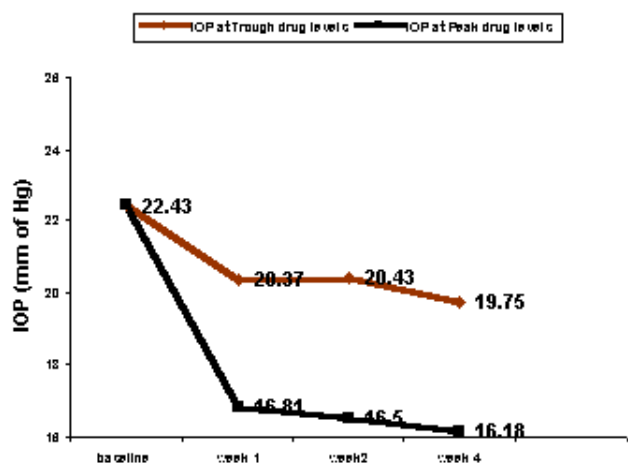
Monotherapy

(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.



Dorzolamide: Adjunctive therapy

(Cipla, Data on file)

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

Parameter	Monotherapy (n=63)	Adjunctive Therapy (n=16)
Ocular stinging	38	4
Ocular burning	17	4
Blurred vision	1	0
Conjunctival hyperaemia	2	0
Tearing	1	0
Dryness of mouth	1	0
Headache	2	0
Allergic reactions	0	0

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 \geq 23 mm Hg)

Follow up visits:

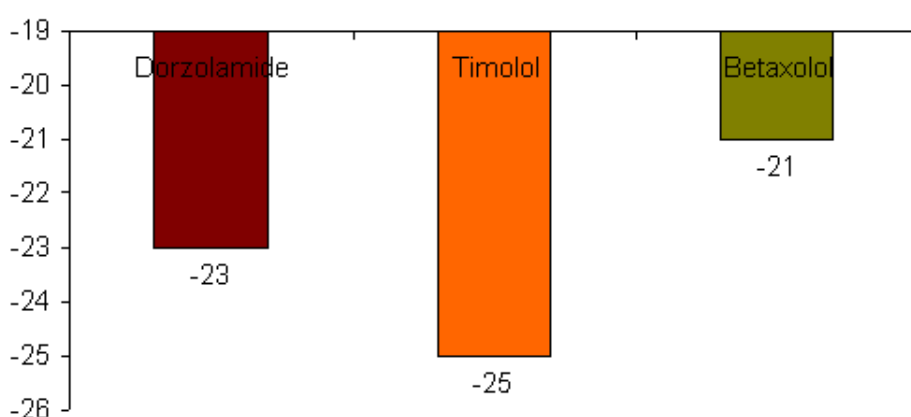
Weeks 2 & 4 and Months 2, 3, 6, 9 & 12

Ophthalmic examinations:

2, 5 & 8 hrs post morning dose (7:30am)

Dorzolamide: Comparison with timolol & betaxolol

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: Comparison with timolol & betaxolol

Conclusion

- Dorzolamide has ocular hypotensive efficacy comparable to beta blockers.
- Dorzolamide was safe and well-tolerated

Dorzolamide: Adjunctive Therapy (To latanoprost) Chart Review

Intraocular pressure reduction at the end of one year by various agents added to Latanoprost (n=73)					
Medication	No. of eyes	Mean baseline IOP (mm Hg)	Mean IOP at one year (mm Hg)	Mean IOP change (mm Hg [%])	P value
Dorzolamide ALL	25	19.8	16.0	-3.9 (19.7)	P <0.001
Dorzolamide BID	11	20.5	16.6	-3.9 (19.4)	P <0.001
Dorzolamide TID	14	19.4	15.5	-3.9 (19.9)	P <0.001
Beta Blockers	23	19.9	17.4	-2.5 (12.3)	P <0.001
Brimonidine	25	21.0	19.0	-2.0 (9.3)	P = 0.0011

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

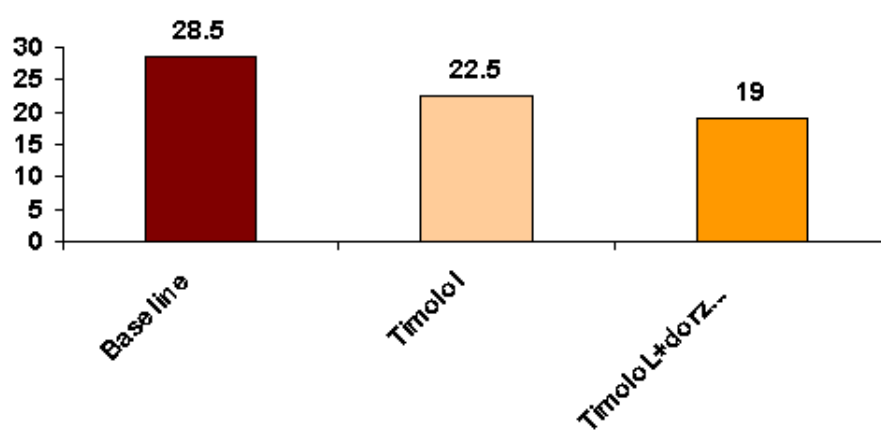
Method

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

Conclusion:

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 ml/min (p < 0.05)

Conclusion

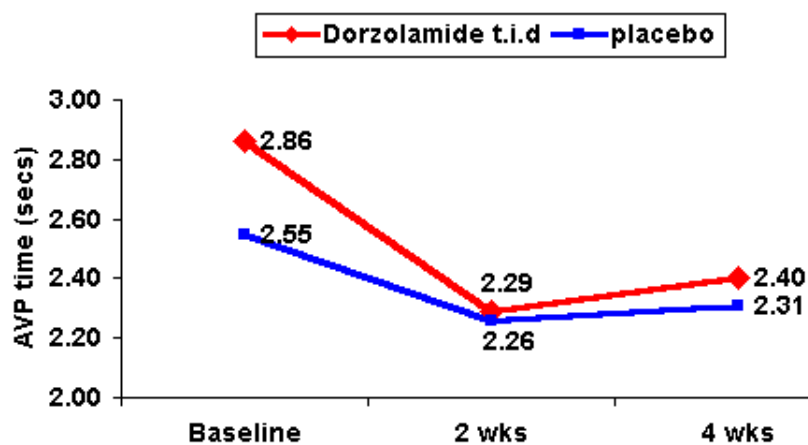
Dorzolamide has a significant effect on visual fields and pOBF in POAG patients and may significantly improve visual function.

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.

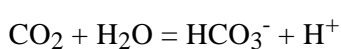
Dorzolamide treatment may benefit optic nerve head preservation by increasing ocular perfusion.

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



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”