Recent Developments in Glaucoma Management

Dr Vinay Nangia
Suraj Eye Institute
559, New Colony
Nagpur MS
440 001
India
Tel: 01-712-2595600, 2595636, 6453332
http://www.surajeyeinstitute.org

This series of talks were conducted by Dr Nangia at the Anatomy Lecture Hall, NSCB Medical College, Jabalpur in conjunction with the Upgraded Dept. of Ophthalmology and the Jabalpur Divisional Ophthalmic Soceity Jabalpur.

The Scientific session was followed by distribution of awards of the JDOS and Quiz Awards.

Medical Management
Overview and Guidelines

Available medications

Betablocker
Pilocarpine
Systemic Carbonic Anhydrase inhibitors
Alpha 2 Agonist
Prostaglandins
Combination Drugs.
Topical CAI

Pressure Reducing Efficacy

Beta Blockers 20-25%
Pilocarpine 20-25%
Systemic Acetazolamine 20-25%
Alpha 2 Agonists 20-25%
Prostaglandins 20-35%
Topical Carbonic Anhydrase Inhibitors 15-25%

Brand Recall -Beta Blockers

(decreases acqueous formation)
Economy
Tried and Tested
20-25% pressure reducing efficacy
Decreases Airflow
Risk of heart disease over long term
Depression

Brand Recall - Alpha 2 Agonists

decreases acq Prod and incr acq outflow
Almost equally effective or less effective than Beta Blockers
Drowsines
A potential friend of the nerve

Brand Recall - Prostaglandins

increases acq. outflow.
Expensive
Ease of use - once a day
25-35% pressure reducing efficacy
Blunts the diurnal variation
'False' Eyelashes
Cosmesis of the iris
Cold Chain

Brand Recall - Pilocarpine

increases outflow
Tried and Tested
Good pressure reducing efficacy
Cheap
Primary Anatomic Drug
Secondary Pressure Reducing Function

Brand Recall - Diamox

decreases acq formation
Reliable pressure reducing efficacy
Very cost effective
Gastrointestinal side effects
Renal side effects
Haematologic side effects.

Brand Recall - Topical CAI

decreases acq. formation
Expensive
Effective
Irritation.

THE PROSTAGLANDINS -OUTFLOW ENHANCERS 'OUR RELATIONSHIP WITH THEM' BIMATOPROST

(bimatoprost ophthalmic solution) 0.03%
First in a new class of ocular hypotensive agents
Bimatoprost 0.03%, citrate/phosphate buffer, pH range 6.8 to 7.8
Contains only 0.005% BAK

No refrigeration Not a prodrug

Represents a New Class of IOP-Lowering Agents:
The Prostamides
Prostamides:
Are members of the fatty acid amide family
Are potent ocular hypotensive agents
Can be synthesized from naturally occurring anandamide
Anandamide pathway believed to be involved in IOP regulation
Activity of Bimatoprost appears to involve a novel prostamide-sensitive receptor
Bimatoprost metabolism
Enzymatic amidase activity, which converts bimatoprost to the corresponding prostaglandin carboxylic acid was found to be present in corneal tissue from human and bovine species.
The hydrolysed product is identical to the free acid of latanoprost with the exception of a double, rather than a single bond at the carbon 13-14 position.

Chemical Structure -Billion Dollar Bonds

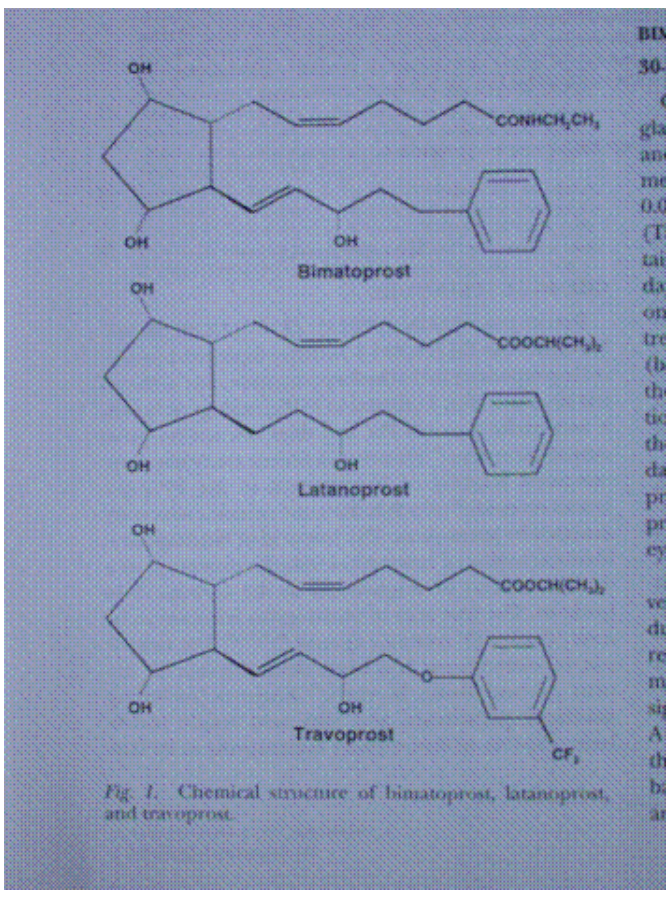

Fig. 1. Chemical structure of bimatoprost, latanoprost, and travoprost.

Latanoprost

PGF2@ isopropyl ester
Selective FP prostanoid receptor agonist
Latanoprost is converted into the active latanoproost acid by ester hydrolysis of latanoprost
Latanoprost is a lipophilic prodrug with enhanced penetration through the cornea.
Cornea functions as a slow release depot for latanoprost acid

Prostaglandin Receptors
The effects of PGF2@ and its analogues are likely mediated by activation of PG receptors.
PG receptor with the greatest affinity for PGF2@ is the FP receptor
Found in ciliary body, iris, and sclera.
Mechanism of Action is
Relaxation of ciliary muscle
Vasodilation
Alteration of 3 dimensional configuration of ECM of ciliary muscle.
Alteration of cytoskeleton of ciliary muscle cells.

PROSTAGLANDIN SIDE EFFECTS

Eye lash growth
Discolouration of iris
Conjunctival Congestion
Cystoid macular oedema
Uveitis
Herpetic activation
Liver Function.
No definite known systemic side effect.
Brand Recall - Prostaglandins
increases acq. outflow.
Expensive
Ease of use - once a day
25-35% pressure reducing efficacy
Blunts the diurnal variation
'False' Eyelashes
Cosmesis of the iris
Cold Chain
Which Prostaglandin

A simplification of the Prostaglandin Selection
Cost
IOP reducing efficacy
Cold chain
redness.

In Advanced POAG,
IOP<15 mm Hg Needed for Stable Vision
Importance of Maintaining Low, Stable IOP
IOP in each individual patient fluctuates during the day and night
Large diurnal IOP fluctuations are a significant risk factor for disease progression
Patients who have periodic or sporadic pressure spikes can lose visual field due to cumulative effects
Diurnal IOP Fluctuations Speed Glaucomatous Progression
Overall Diurnal Mean IOP Bimatoprost and Timolol
Effect of Latanoprost on Circadian IOP
Single dose of latanoprost .005% resulted in sustained and significant reduction of IOP through 24 hours.
It is more effective than timolol 0.5% bid.
.

Latanoprost Pressure Reducing Efficacy over 2 years.

Conclusions

Prostaglandins QD are superior to timolol BID in lowering IOP
Patients receiving Prostaglandins QD achieved very low target pressures
Prostaglandins QD provided diurnal IOP control superior to that of timolol BID
Prostaglanlandins QD is safe and well tolerated
Diurnal IOP Control Latanoprost Vs bimatoprost
at Month 3
Unadjusted Mean IOP Levels by Treatment and Measurement Time at Baseline and Week 12
Intent-to-Treat Population
Medical Treatment of Normal Tension Glaucoma.
Both Latanoprost and bimatoprost are effective in lowering IOP
In patients with normal pressure.
Expect a pressure reducing efficacy of about 20%
Which is very high when you begin with Normal IOP
Latanoprost PRE in patients with Primary Angle Closure Glaucoma.
Mean PRE with Latanoprost was 34.2%
Timolol was 22.6%
Latanoprost added to Pilo and timo in PACG decreased by 21% at 3 months
36% at 12 months
Mechanism of Action.
Paediatric Glaucoma
Children do not respond as well to latanoprost as adults.
Patients with Juvenile glaucoma, and Sturge Weber were found to respond better to Latanoprost.
Assess the response yourself.

Add on Concepts

Primary Drug - most effective role PRE 20-35%
First Add on - Less effective - PRE 10-20%
Second Add on - Least effective -PRE 5-15%
Second add on will have greater efficacy if it replaces first add on drug and greatest efficacy if it becomes primary drug.

Combination Therapy with Prostaglandins

Reported Additional Reduction in IOP
Latanoprost-Timolol 13-37%
Latanoprost-Pilocarpine 2% 7-14%
Latanoprost and CAI 15-24%

REPLACEMENT THERAPY SWITCH/ALTERNATE

Prostaglandins can be used to replace a single ineffective drug
To replace a combination of drugs

REPLACEMENT THERAPY

Prostaglandins may replace a combination of
Beta Blocker and dorzolamide
Prostaglandin and Beta Blocker
Replacement may be equal to or less or more than adding to the existing combination.

Overall Summary - Prostaglandins

Possesses potent ocular hypotensive activity and help patients achieve lower IOPs
Are long acting, allowing once-daily dosing
First line drug, Second line, or Third line
Replacement for single drug or combination
Can be used effectively in a majority of glaucomas
Monocular Therapy Trial (MTT)
This is the use of medication in one eye to get an accurate assessment of its pressure reducing efficacy
Monocular Add on Therapy Trial (MATT)
On a similar principal one may wish to add the second drug to only one eye. This would enable the PRE of the add on drug to be assessed
Monocular Replacement Therapy Trial (MRTT)
Replace the single drug being used with a second drug in one eye. This would enable assessment of the PRE of the replacement drug.
Reverse Concepts - Reverse Calculation (RC)
When a patient is on a single drug, we may use the reverse calculation philosophy to calculate the PRE and therefore arrive at the baseline IOP of the patient before starting the medication
Reverse Concepts - Reverse Monocular Therapy Trial (RMTT)
This involves stopping the drug in one eye and measuring the baseline pressure after the wash out period.
Reverse Concepts - Rediagnosing Glaucoma
When a patient on medical therapy does not seem to have glaucoma on the basis of clinical features, one may stop the medication and reassess and rediagnose the patient.
Excess Glaucoma Therapy