Relatively recent class of drug added to the armamentarium of glaucoma medication.

First discovered in 1930s in prostatic secretion but their IOP lowering effect was identified in 1970s.

First PG analogue to be tried in human was PGF2-tromethamine salt - withdrawn.

First usable PG was develop in Japan – isopropyl unoprostone (Rescula).

First effective PG analog launched in market was latanoprost in 1990s.

First prostamide launched in market was bimatoprost in 1999s.

Family of biologically active class of 20 carbon fatty acid mainly from arachidonic acid.

Autocoids in nature (produced, released & effective locally).

Ocular hypotensive PGs are PGF2 derivative in which heptanoic acid has been converted to either an ester or amide functionally.

Esters are more lipophilic than corresponding acid & penetrate ocular tissue more readily.

Prostanoids analog
- Fatty acid having carboxylate side chains (ester)
- Cell membrane phospholipid
- arachidonic acid
- Strong Prodrug
- Corneal and conjunctival epithelium
- Increasing aqueous humor outflow through uveoscleral pathway
- Decreasing inflow resistance

Prostamides
- Fatty acid having amide side chain
- Naturally occurring phospholipid
- Anandamide
- Weak or no affinity for any receptor
- Biologically active
- Through sclera (85-90%) Reached target tissues directly.
- Increasing aqueous humor outflow through uveoscleral pathway (by 50%) and through trabecular meshwork (by 35%)
- Decreasing inflow resistance

Mechanism of action
- Increases uveoscleral outflow by -
- Relaxation of ciliary body muscle.
- Dilating space between longitudinal ciliary muscle bundle.
- Altering metabolism of extracellular matrix of surrounding ciliary muscle by ECM remodeling.

Properties Latanoprost
- Cmax in aqueous humor 2 hr
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Properties Travoprost

Within 30 min
35-30% (7-8 mmHg)
Stable
Stable at wide range of temperature, refrigeration not needed
Does not require protection from light.
0.004%

Properties Bimatoprost

Within 10 min
27-31% (7-8 mmHg)
Stable
Refrigeration not needed
Requires protection from strong light
0.05%

Latanoprost

Ocular effects
Reduction in IOP occurs within 3-4 hours, peaks within 8-12 hours and persists for up to 24 hours or longer after topical application.
Similar efficacy during day-time and night-time hours
Maximum effect achieved with a concentration of 50 mcg/ml given once daily in the evening
Once daily administration is superior to twice daily (related to the loss of some of the effect due to development of receptor subsensitivity)

When a glaucoma patient instills latanoprost at 9 pm, the maximum IOP lowering effect is after 12 hours i.e. at 9 am (and thats also the time when IOP is at its peak)
Therefore 2 peaks meet i.e. the IOP at its peak and Latanoprost at its peak
Latanoprost when instilled at 9 p.m. effectively lowered IOP at 3, 6 and 9 a.m. at noon at 9 p.m. and at midnight
Latanoprost compared to other agents lead to a fairly uniform circadian reduction in IOP

Advantages of PG Analogues and Prostamides

No effect on blood flow, blood aqueous barrier & retinal vasculature.
No effect on BP, HR, respiratory system, haematology or urine analyses.
Independent of episcleral venous pressure they are DOC in glaucoma secondary to increase episcleral venous pressure.
Additive to any of other antiglaucoma drug.
High pressure lowering effect.
Once daily dosing (in evening).
One of the most tolerable drug with minimal S/E. Duranal variation – very little. No upward drift of IOP over 6 month (long term effect satisfactory). Even if patient miss the doses -- IOP reduction is maintained at 7 mmHg after 1 day. IOP reduction is maintained at 4 mmHg after 3 days.- IOP reduction is maintained at 1.3 mmHg after 14 days.

Indications
As a first line drug in --
Primary & secondary open angle glaucoma.
Normal tension glaucoma.
Glaucoma secondary to increased episcleral venous pressure (EVP) viz Glaucoma secondary to idiopathic elevated EVP
Glaucoma secondary to carotid cavernous fistula.
Glaucoma secondary to A-V shunt/malformation within cavernous sinus
Residual glaucoma following iridotomy in angle closure glaucoma.

Should be avoided in
Neovascular glaucoma.
Glaucoma secondary to Epithelial ingrowths
Extensive iridocorneal – endothelial proliferation.
Inflammatory glaucoma.
Infantile glaucoma.

Side Effects
Most common S/E :-
Conjunctival hyperemia (pink eye) –
Ocular hyperemia is defined as an excessive reddening of the conjunctiva as a consequence of vasodilation.
Compromises the outcome of filtration surgery
Represent a cosmetic problem to the patient thereby leading to noncompliance.
Hyperemia abates by day 5 and to be steady from week 2 up to month 6.
Latanoprost - 5% - 15%
Bimatoprost - 15% - 45%
Travoprost - 35% - 50%

Other common S/E
Foreign body sensation
Eye irritation
SPK
Periocular skin discoloration

Darkening of iris color
More with light colored irides
Due to increased melanosome
Permanent in nature
More with latanoprost

Best avoided in patients who need uniocular therapy particularly in young for cosmetic reason.

Increased growth of eye lashes.

Cystoid macular oedema particularly in patients having
H/O incisional surgery (cataract surgery, vitrectomy).
Retinitis pigmentosa
Active diabetic retinopathy.
* Fundus should be carefully monitored for sign of CME.
* At the first sign of decreased vision drug should be discontinued.
Anterior chamber flare, cells / uveitis.
Relapse of herpes simplex keratitis.

Systemic Side Effects
- Rare
Flu like systems (with latanoprost)
Headache
Myalgia
vaginal bleeding
altered LFT (with bimatoprost).

Contraindications
Active uveitis or H/O recurrent uveitis.
H/O viral corneal ulcer.
H/O incisional surgery.
Inflammatory glaucoma.
Active diabetic retinopathy.
Retinitis pigmentosa.
Pregnancy & lactation.

Drug interactions
Should not be used with pilocarpine (theoretically).
Can be used concomitantly with other topical ophthalmic products.
Additive effect with other antiglaucoma drugs.
Precipitation of drug occur if any other topical medication having thiomersol as preservative is used with latanoprost. Such drug should not be used simultaneously.
Care should be exercised if patient wear contact lenses.
Contact lens should be removed prior to instillation of drops.
Should remain out of the eye for at least 15 minute.