Prostaglandin Associated Periorbitopathy

Tuesday April 3rd 2018

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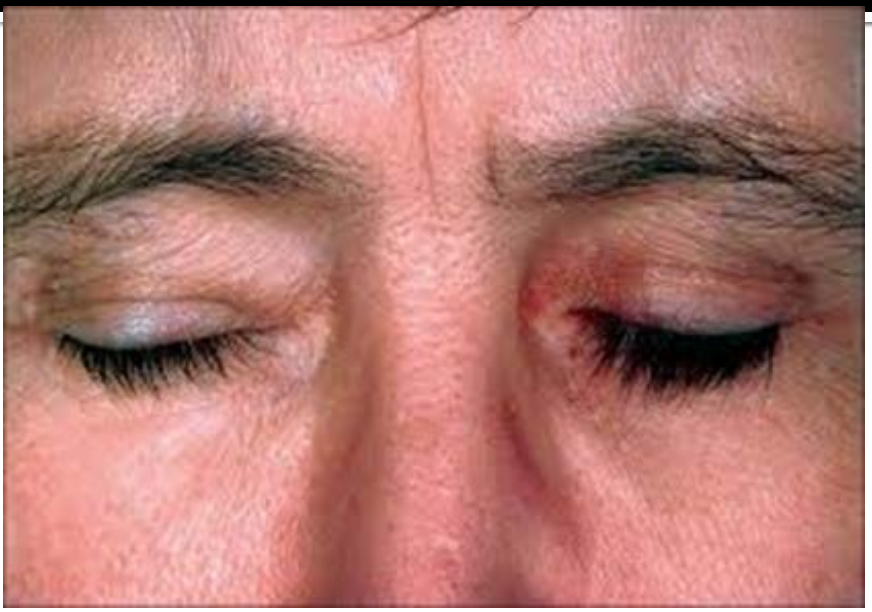
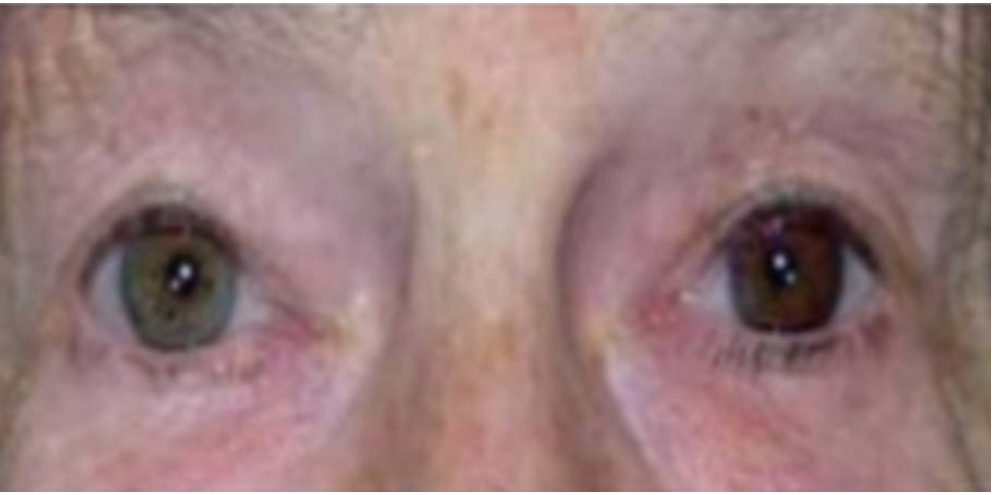
Prostaglandin Analogues

Latanoprost
Travoprost
Bimatoprost
Tafluprost

Side-effects





Conjunctival hyperaemia

Eyelash changes

Iris darkening

Eyelid skin hyperpigmentation

Ocular surface problems

Cystoid macular oedema

Iris cysts

Deepening of upper eyelid sulcus (DUES)

Deepening of lid sulcus from topical bimatoprost therapy.

Optom Vis Sci. **2004** Aug;81(8):574-7.

Peplinski LS, Albiani Smith K.

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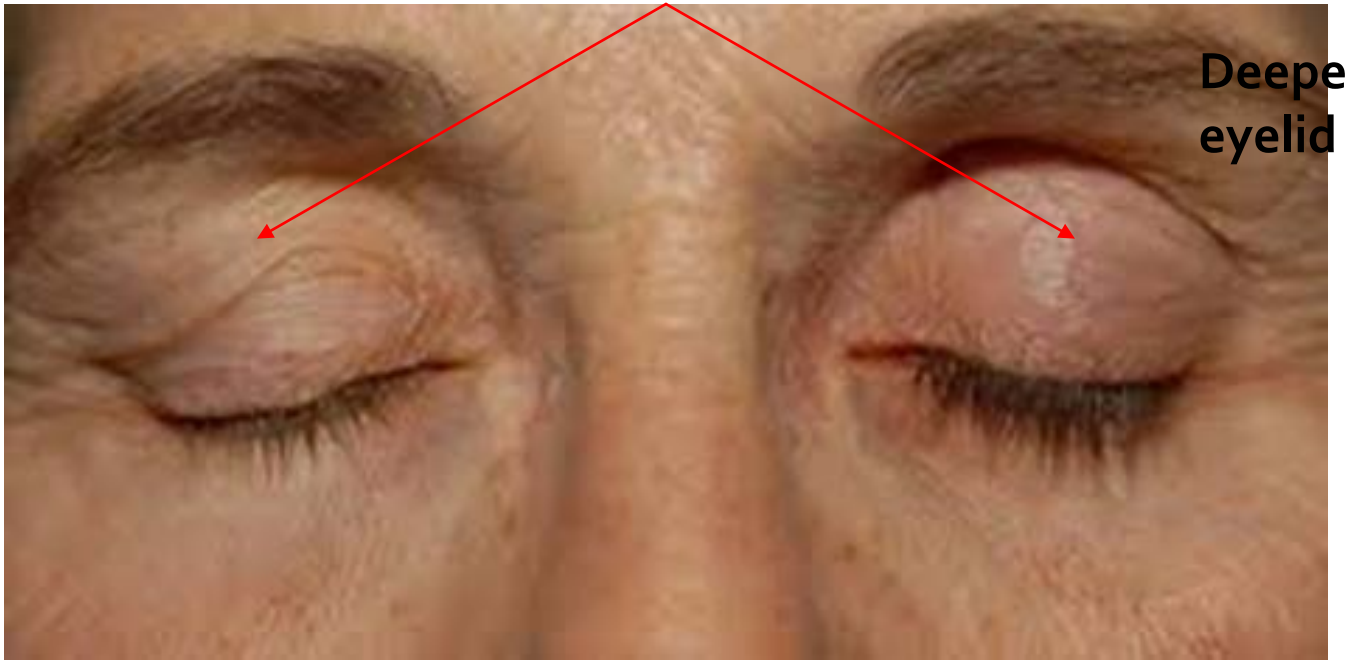
Relative absence upper eyelid dermatochalasia



Deepening upper eyelid sulcus

Deep crease upper eyelid

Prostaglandin Associated Periorbitopathy

Inferior scleral show

Steatoblepharon

Enophthalmos

Tight orbit

Ptosis

Difficulties

Cosmesis – asymmetry/aged *27% noticed changes 15% bothered*

Difficulty IOP measurement
Difficulty during surgery

Compliance

Lagophthalmos
Keratopathy
Exposure keratopathy
Perforation

Orbital fat atrophy causes increased enophthalmos in a supine position with the creation of additional space between the tarsal conjunctiva and cornea.

Factors affecting the development of PAP

Bimatoprost
Travoprost
Latanoprost
Tafluprost

15-60%

+/- Timolol
concurrently or in fixed combination

Incidence within first 4 months may be important

Age *Changes due to aging may be difficult to differentiate from PAP because aging can also lead to orbital fat loss. The only way to differentiate PAP from age related change was to evaluate the change in monocular PGA users.*

Factors affecting the development of PAP

Gender
IOP change
Refraction
Duration therapy
Type of glaucoma

Weight *Overweight individuals tend to have greater orbital fat volumes. The rate of adipogenesis reduction may be affected making it more difficult to detect the appearance of PAP.*

Pathogenesis

- PGA induced lipolysis upon stimulation of PG F-receptor (FP) in orbital tissue.

An in vivo histological analysis indicated that the density of adipocytes obtained from pre-aponeurotic fat biopsies was lowest in bimatoprost treated patients.

- Orbital fat atrophy from inhibition of adipogenesis through FP receptor stimulation.

The activated form of all PGAs dose dependently suppressed adipogenesis in differentiated adipocytes but did not suppress adipogenesis in the adipocytes of FP knockout mice.

Adipocyte differentiation is inhibited through the activation of the FP receptor. Stimulation of the EP_3 receptor is also thought to inhibit adipocyte differentiation Differences in the affinities of the EP and FP receptors for each of the PGAs may influence events in vivo.

Pathogenesis

- The degeneration of smooth muscle fibres due to the reduction of collagens is another means by which PGAs may exert their effects in the orbit.

PGAs reduce IOP by increasing uveoscleral outflow, via a reduction in the levels of collagen types I, III, IV in the ciliary smooth muscles and adjacent sclera. Müller's muscles and the levator palpebrae superioris function as smooth muscles in the upper eyelids, while the posterior layer of the lower eyelid retractor connects to abundant smooth muscles in the lower eyelid.

Timolol

α1-adrenoreceptor agonistic
B2-adrenoreceptor antagonistic

Reduced nitrous oxide production
Mediator of induced hyperaemia
Reduced vasodilating effect
Absorbed less from ocular surface
Have longer act on orbital fat cells

Ptosis

'Ptosis is a characteristic of aging and not PAP which rather causes upper eyelid retraction'.

Unilateral Prostaglandin-Associated Periorbitopathy: A Syndrome Involving Upper Eyelid Retraction Distinguishable From the Aging Sunken Eyelid.

Ophthal Plast Reconstr Surg. 2015 Sep-Oct;31(5):373-8.

Rabinowitz MP, Katz LJ, Moster MR, Myers JS, Pro MJ, Spaeth GL, Sharma P, Stefanyszyn MA.

Ptosis

Lower eyelid retraction is already a well defined feature.
The precise mechanism for ptosis associated with the syndrome was speculative.

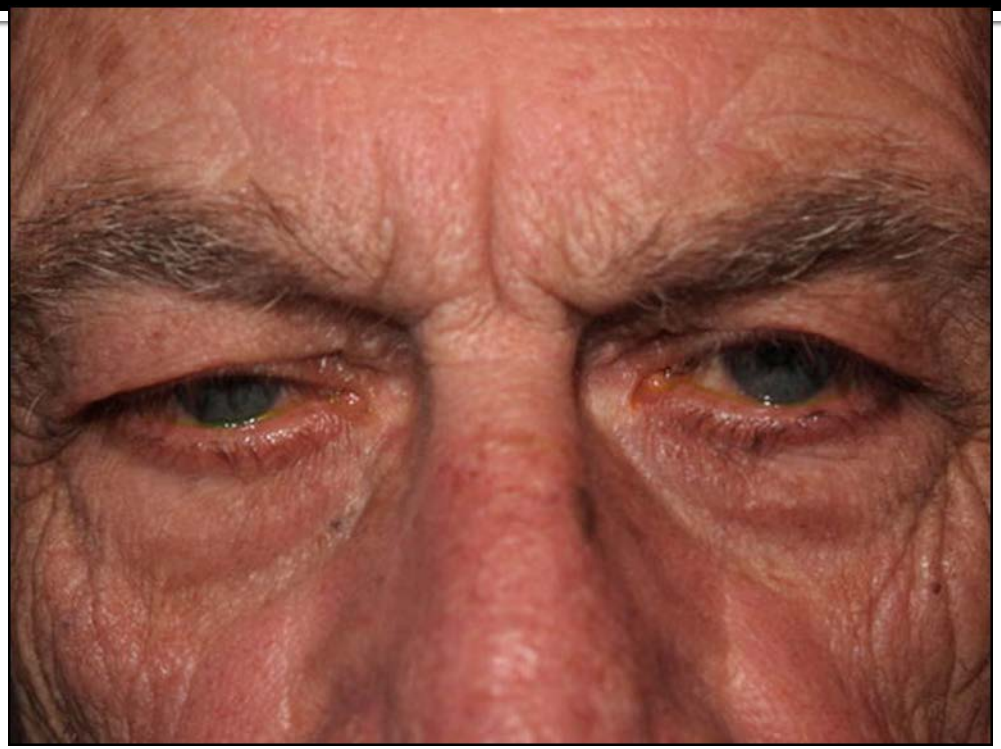
Upper eyelid retraction occurs in the setting of enophthalmos and anophthalmos.

- Sunken sulcus physically pulls the eyelid dorsally into the orbit. Exacerbated by loss of the preaponeurotic fat pad supporting the anterior lamella and orbital septum.

- Inflammation, fibrosis and tightening, complex sympathetic innervation alterations and resultant Müller's muscle overaction are used to explain lid retraction in thyroid eye disease. Each of these has been described within the levator complex, surrounding fat and fascial planes in response to PGAs.

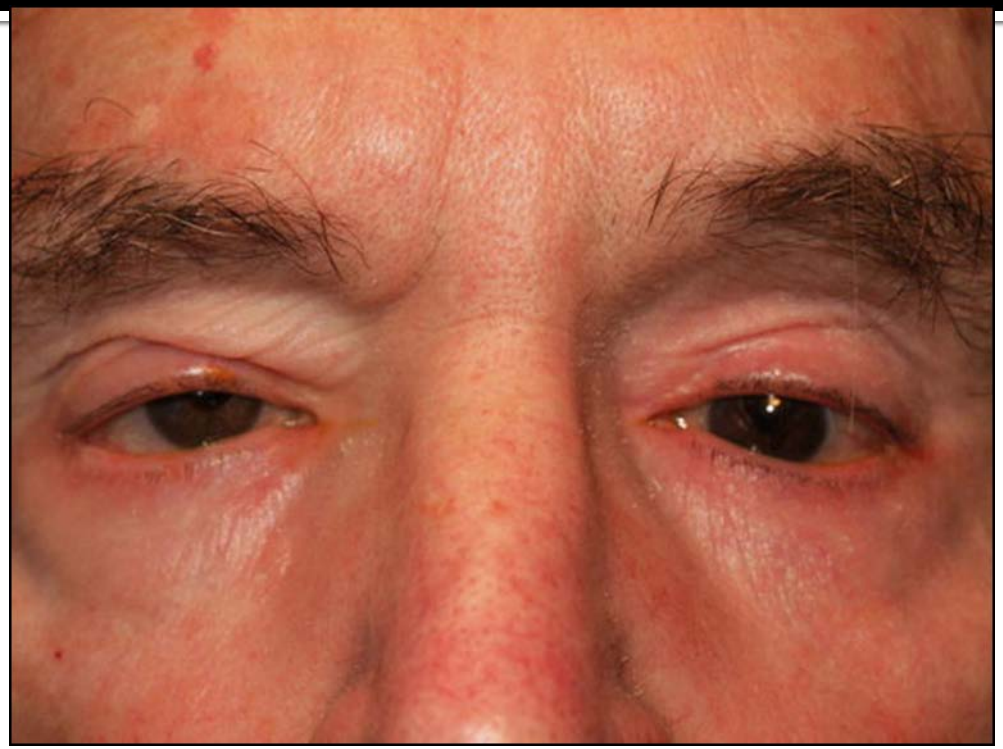
Greatest lid retraction seen in those in which lagophthalmos and redness were the worst.

Grade I PAP



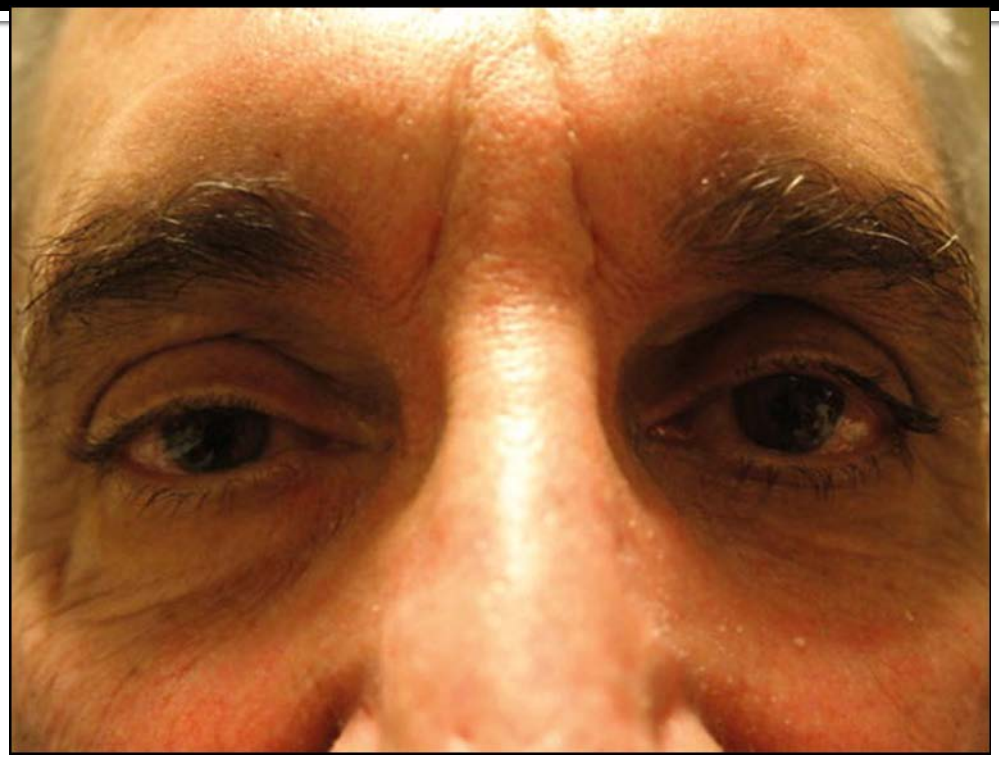
Left. Subtle subjective relative loss of orbital fat **without** superior sulcus deformity. i.e. stage I SSD. There is bilateral brow ptosis and dermatochalasis. Note the relative upper eyelid **retraction** on the treated side.

Grade II PAP



Left. Loss of orbital fat and stage II SSD, in which the superior sulcus is sunken but remains **at** the superior orbital rim. Note the subtle relative upper eyelid **retraction** on the treated side.

Grade III PAP



Left. Loss of orbital fat and stage III SSD, in which the superior sulcus is sunken **posterior** to the superior orbital rim. Note the relative upper eyelid **retraction** on the treated side.

Recovery

Bimatoprost induced deepening of the upper eyelid sulcus reduced or disappeared in 85% those whose treatment was changed to 0.005% latanoprost.

1-6 months

Severe PAP marked by the most significant orbitopathy may be associated with **irreversible** adnexal changes.

Extent and timing of PAP reversal on stopping PGA has never been proven.

Orbital adipocyte apoptosis and not just degeneration may occur causing irreversible fatty degeneration.

In future . . . . .

Pre-treatment evaluation
Observation
Counselling pre-treatment
Unilateral use
New formulations e.g. Monoprost

Thank-you.