Oculoplastics and Glaucoma: Prostaglandin associated Periorbitopathy (PAP)

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Life is full of surprises and so is Medicine. Sildenafil was originally marketed by Pfizer for hypertension and angina but then the "little blue pill" changed the world. Avastin-a drug that was approved by FDA for metastatic colorectal cancer found its way as a miraculous drug for chorioretinal proliferative disorders[1]. Latanoprost a prostaglandin analogue currently used as first line treatment for glaucoma is now also being marketed for lengthening of eyelashes[2].

Prostaglandin analogues associated periorbitopathy (PAP) is a recently described side effect of these antiglaucoma drugs[3]. Earlier reports implicated bimatoprost but lately PAP has been reported as a result of treatment with all topical prostaglandin analogues[4].

The clinical findings associated with PAP are upper eyelid ptosis, deepening of the upper lid sulcus, involution of dermatochalasis, periorbital fat atrophy, mild enophthalmos, inferior scleral show, increased prominence of lid vessels, and tight eyelids. In contrast to previous studies showing ptosis in PAP, relative upper eyelid retraction has recently been reported in most of their patients by Rabinowitz et al[5]. Other known side effects of prostaglandin analogues include lengthening of lashes and increased pigmentation of the iris (See a review article in this issue) and periorbital skin, which could possibly fit under the term PAP as well[6]. Another recent audible sign has been eyelid clicking that was noted intermittently and on each follow-up in each eye when the patient blinked[7].

The prevalence of PAP in Prostaglandin (PG) analogue treated eyes is not known, but anecdotal reports suggest that if we start looking for it, PAP can be identified in almost every patient. A new study by Shah et al[8] designed as a prospective cross-sectional survey using both external photography and external adnexal examination of 157 current, 15 past, and 171 never users of prostaglandin analogues showed that current PG users had a 230-fold increased risk of involution of dermatochalasis and a 249-fold increased risk of incremental loss of lower lid steatoblepharon (herniation of the orbital fat in eyelid). Additionally, upper lid ptosis, levator dysfunction, and lower lid retraction were also highly associated with current prostaglandin use. Levator muscle dysfunction leading to ptosis represent significant side effect that could impact an already compromised visual function in glaucoma patients. Surgery for these malpositions needs to be individualized. Overcorrection of ptosis may result in bleb exposure and the risk of blebitis or endophthalmitis[9].

Pharmacokinetic studies of a single topical administration of 0.1% bimatoprost in animals have shown that eyelid specimens contain more than 2,000 times higher concentrations of bimatoprost compared with aqueous and more than 16 times higher concentrations compared with iris and ciliary body[10]. Thus, there is significant periorbital absorption of prostaglandin analogue medication. Histopathology studies have confirmed that these drugs result in pre-aponeurotic and deep orbital fat atrophy which is most likely the main contributor responsible for the majority of PAP changes[11].

The management of PAP mainly revolves around discontinuation of eye drops, if possible. Otherwise change over from

bimatoprost to latanoprost has also shown reversal of PAP to some extent[12]. While PAP implies pathology or a state of disease, others have reported these changes that can be perceived as an improvement in the overall appearance of the periorbital area beyond eyelash enhancement, induced by the topical application of bimatoprost ophthalmic solution, 0.03% (Latisse®, Allergan, Inc., Irvine, CA). This rejuvenating effect and overall improvement in the appearance of the periorbital area resulting from applying Latisse to the upper eyelid margins has been referred to as "chemical blepharoplasty"[13].

Currently, the use of prostaglandins for cosmetic management of facial fat is under investigation. A prostaglandin topical gel is being tested for dissolving submental fat. Similarly, many studies (including the one at Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan) are being performed currently to demonstrate the beneficial fat atrophy effect of prostaglandin analogues to counteract the changes occurring as a result of Thyroid associated orbitopathy. However so far no results have been published.

Thus, Prostaglandin analogues may produce undesirable effects for some while these may be beneficial cosmetically for others. Why not to change the term Prostaglandin-Associated Periorbitopathy (PAP) to Prostaglandin-Associated Periorbital Remodeling (PAPR).