

# Eyelash Hypertrichosis in a Patient Treated With Topical Latanoprost

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*We describe a female patient with a history of primary open-angle glaucoma who, following treatment with topical latanoprost, a synthetic prostaglandin  $F_{2\alpha}$  analog, developed hypertrichosis of the eyelashes. Hypertrichosis, a recently described side effect of latanoprost—together with iridal pigmentation—represents a potentially permanent cosmetic side effect associated with the use of this highly effective intraocular pressure-lowering agent. The molecular mechanism underlying latanoprost-induced hypertrichosis is unknown.*

Latanoprost is a topically applied prostaglandin  $F_{2\alpha}$  ( $PGF_{2\alpha}$ ) analog recently shown to be highly effective in the management of chronic open-angle glaucoma.<sup>1</sup> Latanoprost reduces intraocular pressure (IOP) by increasing uveoscleral outflow. Unlike the action of traditional ocular hypotensive agents such as timolol, latanoprost does not affect the production of aqueous humor.<sup>2</sup> The advantages of latanoprost include not only its highly effective ocular hypotensive effect, which is superior to that of timolol,<sup>1</sup> but also its very favorable side effect profile. More important—and in contrast to timolol—topical latanoprost lacks any detectable systemic side effects because of both its lower once-per-day dosing and very short pharmacologic half-life in the circulation (<20 minutes).<sup>3</sup> Initial phase III studies on latanoprost revealed local ocular side effects, such as superficial punctate keratopathy, conjunctival hyperemia, and iridal color change (also called *prostaglandin-induced iridal pigmentation* [PIIP]).<sup>1</sup> PIIP occurs in 11% to 23% of patients using latanoprost and represents a permanent alteration in iri-

dal color believed to be secondary to increased melanin production in the melanocytes of the iris stroma.<sup>4</sup> We report the case of a patient who displayed eyelash hypertrichosis a more recently recognized side effect of latanoprost therapy. The occurrence of increased local eyelash growth and pigmentation in patients treated with latanoprost is a novel and unexpected side effect of  $PGF_{2\alpha}$ .

## Case Report

A 72-year-old white female with an 8-year history of primary open-angle glaucoma developed progressive visual field loss and glaucomatous optic nerve cupping with uncontrollable IOP, despite maximally tolerated medical therapy and previous argon laser trabeculoplasty in both eyes. The patient underwent trabeculectomy in the left eye in July 1996, which resulted in such significant improvement in IOP that topical therapy in that eye was discontinued.

Though the patient's right optic nerve showed evidence of only minimal glaucomatous damage, the IOP in that eye was elevated to an unacceptable level, despite a regimen of levobunolol 0.5%, pilocarpine 4%, and dorzolamide 2%. Latanoprost 0.002% was added to her therapeutic regimen with modest improvement. Within a few months, the patient noted that the eyelashes of both eyelids had become longer, thicker, and more numerous.

Further elevation of the IOP in her right eye over the next few months necessitated a trabeculectomy. However, the hypertrichosis persisted even after all topical glaucoma therapy was discontinued. In addition, the patient reported new vellus hair growth on her right earlobe.

## Comment

Since latanoprost's approval as a standard ocular hypotensive agent, hypertrichosis and increased pigmentation of the eyelashes have been noted in a series of patients with glaucoma who were treated with topical latanoprost. These patients exhibited an increased

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number of eyelashes, with some individuals displaying additional rows of eyelashes in both upper and lower eyelids of the treated eyes. Latanoprost-treated eyes displayed the new growth of lashlike hair in areas adjacent to the region of normal eyelash distribution. Furthermore, latanoprost therapy appeared to increase eyelash pigmentation, length, and thickness.<sup>5</sup> Wand<sup>6</sup> reported that treatment with unilateral topical latanoprost 0.005% to the left eye of a 65-year-old woman with open-angle glaucoma resulted in thicker, darker, and more numerous eyelashes limited to the treated eye. Subsequent treatment of the right eye induced similar eyelash pigmentary changes over an 8-week period.<sup>6</sup>

We report the development of hypertrichosis in an older patient with open-angle glaucoma who received topical latanoprost to only one eye but increased eyelash growth bilaterally. We also observed increased vellus hair growth on the right earlobe. Both bilateral hypertrichosis in the setting of the unilateral treatment and increased hair growth on the earlobe are somewhat perplexing, implying that either systemic absorption of latanoprost occurs, which induces hair growth in other sites, or the possibility that the patient unknowingly applied the drug topically to these other sites. An increase in pigmentation of the eyelashes was not seen, but such an effect, much like PIIP, may be restricted to a minority of treated individuals.

The prostanoid family of molecules, including prostaglandins  $D_{2\alpha}$ ,  $E_{2\alpha}$ ,  $F_{2\alpha}$ , and  $I_{2\alpha}$  and thromboxane  $A_2$  (TXA<sub>2</sub>), functions as either autocrine or paracrine factors with diverse biological activities.<sup>7</sup> Only cells that bear prostanoid receptors, designated DP, EP, FP, IP, and TP, are responsive to a given prostanoid molecule. The receptors, recently cloned and sequenced, belong to the family of G protein-coupled cell surface receptors. Interaction between a prostanoid and its receptor initiates an intracellular signaling response, characterized by an increase in the formation of diacylglycerol and inositol trisphosphate, with both subsequent activation of protein kinase C and mobilization of intracellular calcium.<sup>8</sup>

The FP receptor to which latanoprost binds<sup>9</sup> can be shown by immunohistochemistry and in situ hybridization to be expressed in all ocular tissues, including corneal epithelium, pigmented and unpigmented epithelial cells, iris, retina, optic nerve, and lens epithelial cells.<sup>8</sup> Examination of the eyelash hair follicles reveals a population of cells that express the

FP receptor, and thus would represent the putative targets of latanoprost-induced hypertrichosis and hyperpigmentation. The mechanism by which latanoprost initiates increased eyelash pigmentation may be similar to the augmented melanogenesis associated with PIIP.<sup>3</sup>

Further study of latanoprost may reveal cellular and biochemical effects of PGF<sub>2 $\alpha$</sub>  within the eyelash hair follicle that closely resemble this prostanoid's influence on cells in culture. Additionally, chronic treatment with latanoprost, when administered either locally or systemically, perhaps affects the behavior of cells within the hair follicles found at other body sites. This effect of latanoprost may provide an additional tool for further understanding of both hair growth and pigmentation and the biology of cellular proliferation and differentiation.

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