Introduction

Travoprost is a synthetic prostaglandin F₂α (PGF₂α) analog and a high-affinity agonist for selective prostaglandin receptors. It is an ocular hypotensive, lipid-soluble agent that decreases the intraocular pressure (IOP) by increasing the uveoscleral outflow.¹ Travoprost 0.004% (Travatan, Alcon, Irvine, CA, USA) has several well-known side effects, namely, conjunctival hyperemia, ocular irritation, iris pigmentation, eyelid skin darkening, and eyelash hypertrichosis.¹ However, there are no reports of a deepening of the eyelid superior sulcus associated with its use.

Case Reports

Case 1

A 66-year-old Korean woman was diagnosed with unilateral normal-tension glaucoma and was started on travoprost 0.004% in the right eye at bedtime. She had a follow-up examination every 3 months. A mild eyelid erythema developed after 1 month of travoprost, but she tolerated this alteration well, so the topical travoprost was continued.
Two years later, the patient stated that she had noticed a recent sunken appearance of the right eyelid, which resulted in a disparity in the appearance of the two eyes.

On examination, she had a mild hyperpigmentation of the upper eyelid and a deepening of the eyelid superior sulcus of the right eye. A clinically significant disparity of eyelid configuration was apparent between the eyes. The right eyelid showed mild ptosis with a higher skin crease than the fellow eye. The margin reflex distance (MRD1) was +0.5 in the right eye and +3 in the left eye. The levator functions were otherwise good and symmetrical in both eyes, but with evidence of unilateral levator dehiscence or weakening of the right eyelid.

Slit-lamp examination showed no significant conjunctival injection or other complications in the right eye. Because the IOP was well controlled and the patient was not unhappy about the appearance, travoprost monotherapy was continued in the right eye (Fig. 1, top left, top right, bottom left). Twelve months later, the deepening of the eyelid superior sulcus and aponeurotic ptosis of the right eye was not altered, and there was a significant disparity between the eyes (Fig. 1, bottom right).

**Case 2**

A 67-year-old Korean man who was diagnosed with unilateral primary open-angle glaucoma was started on travoprost 0.004% in the left eye. He had a follow-up examination every 3 months. His IOP was well controlled, and there were no specific adverse effects except moderate eyelid skin darkening. At the 2-year follow-up visit, he complained of a marked eyelid disparity, with a sunken eye appearance and darkening of the left eyelid.

On examination, he had eyelid hyperpigmentation, hypertrichosis of the eyelashes, and deepening of the eyelid superior sulcus of the left eye. The MRD1 was +2 in both eyes, and levator function was good and symmetrical. The crease in the upper eyelid was slightly higher in the left eye, but the skin above the tarsal plate did not appear to be thin or semitransparent. The lower eyelid of the right eye had a baggy appearance suggesting a palpebral fat herniation, but the left eye was definitely not baggy. A significant asymmetry of eyelid configuration was apparent between the eyes (Fig. 2, top left, middle left, bottom left).

The patient preferred to discontinue the drug, so 2.0% dorzolamide–0.5% timolol mixed ophthalmic solution (Cosopt, MSD, Whitehouse Station, NJ, USA) was substituted for travoprost. After 6 months, hyperpigmentation and hypertrichosis of the upper eyelid had slightly decreased in the left eye, but the eyelid superior sulcus deepening did not change. The lower eyelid palpebral fat of the left eye had slightly increased, but was still less baggy than the fellow eye (Fig. 2, top middle, center, bottom middle). Fifteen months after discontinuation of travoprost, the upper eyelid hyperpigmentation and sulcus deepening had much improved in the left eye. The lower eyelid palpebral fat in the left eye had increased after discontinuation of travoprost, but was still less baggy than the fellow eye. (Fig. 2, top right, middle right, bottom right).

**Comments**

A deepening of the eyelid superior sulcus after topical drug use has been reported only after topical bimatoprost. The deepening is also prominent after travoprost use, and no other drug has been reported with this side effect. The deepening of the eyelid superior sulcus causes a disparity in the appearance of the eyes and can be the main reason for discontinuing topical travoprost. Monocular use can lead to asymmetrical eyelid appearance, causing significant cosmetic problems. These findings seem to be more significant in Asians, because a deep superior eyelid sulcus is not common in Asians in whom the levator complex is inserted low onto the tarsus. In addition, Asians seldom have an eyelid crease or a deep sulcus.

The photographs of our patients can be compared with those of Caucasian patients with the same complications after topical bimatoprost. The sulcus deepening is more striking in Caucasians because of a preexisting deep eyelid sulcus (presumed by the fellow eye). However, the incidence and exact mechanism for this side effect are unknown.

To exclude conditions that may have contributed to the unilateral superior sulcus deepening, a careful history and physical examination were performed. Neither patient had a history of eyelid trauma, contact lens use, or upper or lower blepharoplasty. The exophthalmometry values were not significantly different between the eyes, excluding the possibility of a contralateral exophthalmos. The pupillary reflexes and ocular motility were normal in both cases.

In the first case, the eye using topical travoprost showed a unilateral aponeurotic ptosis, but in the second case, levator dehiscence was not definite. Aponeurotic ptosis is mainly caused by either an involutorial levator dehiscence or atrophic changes, which are bilateral and symmetrical in most cases. An aponeurotic ptosis has also been reported after long-term hard contact lens wear, and the mechanism for the levator dehiscence is mechanical, namely, the pulling of the lids laterally at the lateral canthus followed by a harsh blink. After many years of repeated mechanical rubbing of the upper eyelid and levator complex, a levator aponeurosis dehiscence, with histological features of mild fibrosis of Mueller muscle or fatty degeneration of the aponeurosis and Mueller muscle, can develop. This may also explain the present cases, that is, the repeated stretching of the upper eyelid during topical drug instillation can result in levator dehiscence and eyelid superior sulcus deepening. However, because other topical drugs used more frequently (e.g., >2 times/day) are not known to develop such side effects, it is more likely that the specific effects of travoprost contributed to the eyelid sulcus deepening.

The second proposed mechanism, which would make the levator complex more vulnerable to mechanical insult, may be fatty degeneration and reduced collagen fibers of the