

Letter to the Editor

Does timolol LA enhance the disrupting effect of travoprost on the blood–aqueous barrier?

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doi: 10.1111/j.1600-0420.2005.00618.x

Editor,

A 43-year-old white man referred as a glaucoma suspect was found to have intraocular pressure (IOP) of 24 mmHg OD and 14 mmHg OS. He had no past history of any injury, surgery or inflammation. He was in good health and did not take any medication. Anterior segments were unremarkable and gonioscopy showed grade IV open angles (Shaffer system). Fundoscopy showed discs with a cup/disc ratio of 0.9 OD and 0.5 OS. There was definitive glaucomatous field loss in the right eye. He was started on guttae travoprost nocte in the right eye. During subsequent follow-ups, his IOP in the left eye was also found to be elevated (32 mmHg) and he was advised to use the drops in both eyes. Timolol LA was added later in the left eye, as the IOP remained raised.

Three months after the introduction of timolol LA, the subject's left eye showed signs of anterior uveitis with keratic precipitates, moderate flare and moderate cells (++) . Intraocular pressure was 19 mmHg in both eyes. Gonioscopy and fundoscopy showed no change. Travoprost-induced anterior uveitis was suspected and the drug was stopped in the left eye but timolol LA was continued. No anti-inflammatory or steroid drops were prescribed. A review 3 weeks later showed complete resolution of uveitis. The left eye was rechallenged with travoprost (with the patient's permission), leading to the recurrence of the uveitis, which again resolved spontaneously on stopping the drug. Intraocular pressure remained at 19 mmHg during this and subsequently.

Travoprost is an isopropyl ester pro-drug with high affinity and highly selective FP prostaglandin agonist action. Prostaglandin analogues stimulate the release of PGE₂ (Yousufzai & Abdel-Latif 1996), which in turn activates phospholipase II to release arachidonic acid and, subsequently, pro-inflammatory eicosanoids. Several cases of latanoprost-induced uveitis have been reported (Fetchner et al. 1998). Laser flare meter studies have shown that travoprost induces less flare and cells compared to latanoprost (Cellini et al. 2004). This is because travoprost has the higher affinity and highly selective affinity to FP receptors and minimal affinity for EP receptors (Sharif et al. 2003). Previously published case reports describe travoprost-related uveitis in patients with prior intraocular surgery (Faulkner & Burk 2003; Kumarasamy & Desai 2004), one of whom had pseudoexfoliation (Kumarasamy & Desai 2004), both situations known to alter the blood–aqueous barrier. However, our patient did not have any predisposing conditions that might have altered the blood–aqueous barrier. His uveitis resolved simply on stopping travoprost, and recurred on rechallenge. Hence, the uveitis is likely to have been drug-related and not to have arisen from other causes.

Why did this patient develop uveitis only in the left eye, although he was on travoprost for both eyes? Did timolol LA drops have any role in this event? Timolol LA is a gel-forming solution of timolol maleate that contains potassium sorbate to enhance the bioavailability of the timolol and half the usual dose of its preservative, benzalkonium chloride.

A study by Miyake et al. (2001) showed enhanced disruption of the blood–aqueous barrier caused by timolol and bezalkonium chloride. The authors surmised that benzalkonium chloride, rather than timolol, was the main contributing factor. However, this study was carried out soon after cataract surgery. Another study on the benefit of travoprost adjunctive therapy with timolol 0.5% did not find any clinically relevant or statistically significant aqueous flare or inflammatory cells with this combination (Orengo-Nania et al. 2001). However, a combination of timolol LA and travoprost could increase the drug-related damage to the blood–aqueous barrier.

Therefore, it is likely that, in our patient, the combined effect of travoprost and the prolonged effect of either the timolol or the preservative benzalkonium chloride in timolol LA disrupted the blood–aqueous barrier, causing unilateral uveitis.

In conclusion, this case is unique in that travoprost-induced uveitis developed unilaterally in a healthy eye.

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