

Timolol maleate superior to timolol hemihydrate in trial

Anterior chamber, AUC concentrations better, according to penetration research

By Nancy Groves

Reviewed by Leon W. Herndon, MD

Durham, NC—A proprietary formulation of timolol maleate ophthalmic solution 0.5% (Istalol, ISTA Pharmaceuticals) exhibited superior anterior chamber concentrations at a series of time points from 15 to 180 minutes when compared with a proprietary formulation of timolol hemihydrate ophthalmic solution 0.25%/0.5% (Betimol, Vistakon Pharmaceuticals). The timolol maleate solution also had nearly double the area under the curve (AUC) concentration versus the timolol hemihydrate solution from 0 to 3 hours, according to recent data collected from a penetration study conducted in an animal model.



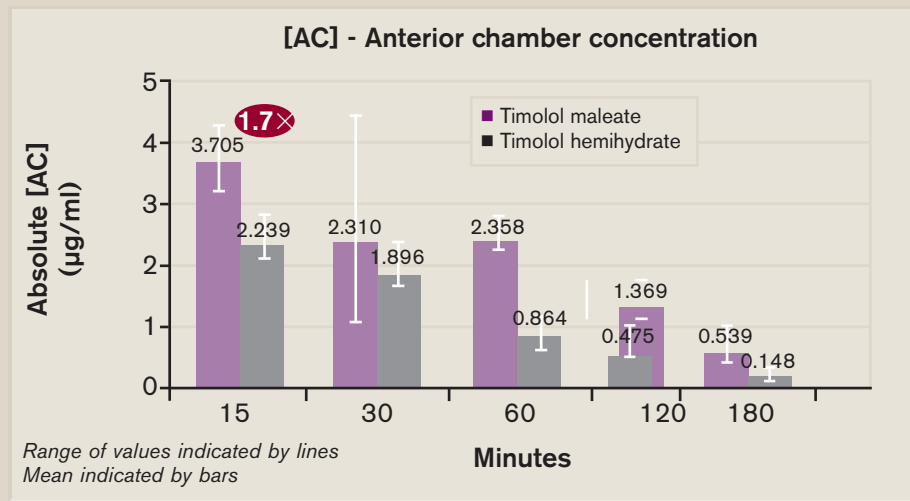
Dr. Herndon

In a study using 30 male albino rabbits, anterior chamber concentrations of the timolol maleate solution were higher at all time points (15, 30, 60, 90, and 180 minutes) than those of the timolol hemihydrate solution and were more than double at 60, 90, and 180 minutes (2.4 versus 0.9 µg/ml, 1.4 versus 0.5 µg/ml, and 0.5 versus 0.1 µg/ml, respectively). The AUC of the timolol maleate formulation was 10.3 µg/h/ml versus 5.6 µg/h/ml for the timolol hemihydrate formulation. The study was

Take-Home Message

The corneal penetration of a proprietary formulation of timolol maleate ophthalmic solution 0.5% (Istalol, ISTA Pharmaceuticals) is significantly greater than that of a proprietary formulation of timolol hemihydrate ophthalmic solution 0.25%/0.5% (Betimol, Vistakon Pharmaceuticals) although both drugs are forms of timolol. Better penetration is correlated with improved safety and efficacy, considerations that are part of the selection of a beta-blocker for control of IOP.

Figure 1 Penetration



Ophthalmology Times / Source: ISTA Pharmaceuticals

Figure 1 Superior anterior chamber concentrations were seen with the timolol maleate solution when compared with the timolol hemihydrate solution.

performed by ISTA, makers of the timolol maleate solution, and produced results similar to those of an earlier study, also done in rabbits.

"With the new formulation of [timolol maleate], we are seeing better corneal penetration and less systemic absorption. That's what makes [this solution] a safer formulation of timolol," said Leon W. Herndon, MD, associate professor of ophthalmology, Duke University Eye Center, Durham, NC.

Distinctions

Although both agents are forms of timolol, there are distinctions between them.

"The difference is that [the timolol maleate formulation] is combined with sorbic acid, leading to a compound that enhances the lipophilicity of timolol, so I think this [timolol maleate] solution is a big improvement for our patients," Dr. Herndon said.

In addition, the timolol maleate formulation is the only beta-blocker solution indicated for once-daily dosing, he added. The usual starting dose of the timolol hemihydrate formulation is one drop in the affected eye twice a day, although it may be reduced to once a day when IOP is maintained at a satisfactory level.

This information is helpful to clinicians when deciding which beta-blocker to prescribe, Dr. Herndon said.

"You want to emphasize safety and efficacy," he added.

"Beta-blockers have an extensive side-effect profile, so for the right patient, I think that [timolol maleate] is safer. It's absorbed into the anterior chamber much more readily than it is into the systemic circulation, so you'll have much lower serum concentrations than you would with timolol hemihydrate and, therefore, it should be a safer medication. This new formulation of timolol maleate is my timolol of choice just based on the safety aspect of it, and it's proven to be as effective as regular timolol, so why not choose it?" he added. **OT**

FYI

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