THE RETURN OF PILOCARPINE

Reflections on uses past and present.

BY I. PAUL SINGH, MD

Pilocarpine was a mainstay of medical glaucoma therapy before the advent of prostaglandin analogues in the 1990s. The drug was effective for achieving significant IOP reductions in several groups of patients, including those with primary open-angle glaucoma, pigmentary glaucoma, steroid-induced glaucoma, and even angle-closure glaucoma.

Because of its short half-life, pilocarpine typically had to be administered four times per day; this dosing schedule placed a significant burden on patients and resulted in challenges with compliance. Further, high concentrations (≥ 4%) of pilocarpine were used to treat glaucoma. With these concentrations dosed frequently over time, prolonged pupillary constriction and poor dilation accompanied pilocarpine's early use. Understandably, the drug fell out of favor when newer classes of medication with longer durations of action and better tolerability emerged.

BACK, BUT DIFFERENT

In 2021, the FDA approved the first pharmacologic treatment for presbyopia. Vuity (pilocarpine HCl ophthalmic solution 1.25%, Allergan) is a low-concentration formulation of pilocarpine in a customized vehicle with proprietary technology designed to optimize its delivery.

Vuity does not tend to constrict the pupil as tightly as did concentrations of pilocarpine administered four times daily in the past. Movement of the iris or the pupil in general is still possible. Additionally, Vuity's duration of action is up to 6 hours. Because the pupil returns to its native state daily when the drug wears off, the risk of chronic pupillary constriction theoretically should be lower than with past use of pilocarpine.

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The vehicle for pilocarpine delivery in glaucoma was not optimized for absorption and patient comfort. The vehicle can play a pivotal role in the bioavailability, tolerability, and overall efficacy of any drug. Manufacturers are forced to place pilocarpine in an acidic environment to maintain its stability and concentration (bioavailability). As a result, patients with glaucoma experienced significant burning, hyperemia, and even headaches with the use of pilocarpine. With the vehicle technology in Vuity, the drug rapidly adjusts the physiologic pH of the tear film once instilled; this increases corneal penetration, allowing less drug to reside on the surface, thus increasing safety and decreasing tolerability issues.[1-3]

A COMMON THREAD

With the pilocarpine used today, advances in design and delivery have decreased side effects and enabled a lower concentration of drug to be used while allowing the pupil to return regularly to its native state. These nuances are important to differentiate between pilocarpine for glaucoma and pilocarpine for presbyopia.

As with all treatments, it is important to set appropriate patient expectations for tolerability and treatment effect with Vuity. I tell patients that it may take about a week before they experience the desired range of vision because the brain needs time to adapt to the smaller pupillary aperture.

Repurposing medication for different conditions or diseases is a common thread in the history of medicine, but advances in formulation and delivery can have a significant impact on patient experience and compliance. ■

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