Voriconazole Treatment of Fungal Scleritis and Epibulbar Abscess Resulting From Scleral Buckle Infection

Fungal infections, both ocular and systemic, can be difficult to treat. Challenges include the difficulty of diagnosis, possibly diminished host immune response, drug resistance of organisms, the difficulty of drug penetration, and the limited number of antifungal agents.

Voriconazole (Vfend; Pfizer Pharmaceuticals, New York, NY) is a new triazole antifungal agent; potent and wide-ranging activity has been demonstrated in vitro and in clinical studies.1-6 In May 2002, oral and intravenous formulations of voriconazole were approved by the US Food and Drug Administration for primary treatment of acute invasive aspergillosis and for salvage therapy for infections caused by *Scedosporium apiospermum* and *Fusarium* species. As with other azole compounds, the primary mode of action of voriconazole is the inhibition of cytochrome P-450–mediated 14-α-lanosterol demethylation, which is an essential step in fungal ergosterol biosynthesis.

Based on a MEDLINE search, we believe that this is the first case report of refractory fungal scleritis with a nodular epibulbar abscess due to scleral buckle infection that was successfully treated with voriconazole, and the first report of intraocular concentration of voriconazole in a human following oral administration.

Report of a Case. A 65-year-old immunocompetent woman sought treatment for a hyperemic and tender left eye associated with an inferonasal epibulbar nodule. According to the patient, the nodule began “like a pimple” but gradually grew during the preceding 2 months. During the past year, the patient had undergone 3 procedures at another facility for recurrent retinal detachments, including pars plana vitrectomy and a scleral buckling procedure. She had been given subconjunctival methylprednisolone acetate at the conclusion of each operation, and postoperative topical prednisolone acetate was continued for 2 to 3 months each time. On examination, visual acuity was hand motions OS. She was aphakic, and the retina was attached, with areas of preretinal fibrosis and chorioretinal scarring. Areas of peripheral scleral thinning were noted. The nodule was only minimally mobile and slightly tender, but the inferonasal sclera was particularly tender and erythematous (Figure 1).

Surgical exploration revealed that the nodule was an abscess. The scleral buckle was initially not disturbed because of significant necrosis of the sclera and the risk of globe rupture. Cultures yielded *Aspergillus fumigatus*, and topical 0.15% amphotericin B and oral ketoconazole were initiated. After a lack of clinical response to a 4-week course of therapy, itraconazole was substituted for ketoconazole in hopes of improving intraocular penetration. A continued lack of clinical improvement led to uncomplicated scleral buckle removal 1 month later. During the next 4 months, despite multiple debridements and continued use of topical amphotericin B and oral itraconazole, the infection continued to spread counterclockwise around the eye (Figure 2). After learning of the investigational use of voriconazole, we obtained institutional review board approval of voriconazole use on a compassionate basis. Other antifungal agents were discontinued, and treatment with oral voriconazole, 200 mg twice a day, was begun. After 1 week of treatment, ocular tenderness and left-sided headache disappeared. Redness of the eye improved during the next 3 months (Figure 3).

During the second month of therapy, simultaneously acquired serum and intraocular fluid samples were assayed for trough concentra-

Figure 1. The patient’s left eye at the initial examination shows an inferonasal epibulbar mass and hypertropia due to mass effect.
tion of voriconazole by Pfizer Central Research (Kent, England). The serum concentration was 1.619 µg/mL, and the intraocular concentration was 0.865 µg/mL. Voriconazole was discontinued after 4 months of treatment, when the eye appeared to have fully recovered from the fungal infection. During 24 months of follow-up, there was no evidence of recurrence, and the patient underwent uncomplicated secondary intraocular lens implantation (Figure 4). She noted that her onychomycosis had also improved markedly while she was taking voriconazole.

Comment. The first report of the efficacy of voriconazole in the treatment of a human ocular fungal infection described a case of ulcerative keratitis caused by *Fusarium solani*.

In that report, successful treatment required intravenous, oral, intracameral, and topical routes with voriconazole. All routes of administration were well tolerated by the patient. In our patient, oral treatment alone was effective, despite the usual difficulty in treating scleritis with oral agents because of the relatively avascular nature of sclera. Intraocular concentra-
Voriconazole was above the MIC90 (minimum inhibitory concentration) of 0.5 µg/mL for A fumigatus reported in various studies. Voriconazole also has been shown to be effective for endogenous Fusarium endophthalmitis and Paecilomyces lilacinus endophthalmitis.

In larger clinical studies of systemic fungal diseases, the most commonly reported adverse effects of voriconazole were transient visual disturbances, including brightness, blurring, light sensitivity, or altered color perception. These visual abnormalities were reported in approximately 30% of patients receiving voriconazole, typically began 30 minutes after dosing, and lasted about 30 minutes. Other adverse effects included elevated liver enzyme levels and facial erythema. The ability to achieve effective intraocular drug concentrations with oral administration, the broad spectrum of antifungal activity, and the relatively low level of systemic adverse effects suggest that voriconazole may have a wider role in the future for treatment of ocular fungal infections.

Judy E. Kim, MD
Stephen L. Perkins, MD
Gerald J. Harris, MD
Milwaukee, Wis

The authors have no relevant financial interest in this article.

This study was supported in part by unrestricted grant from Research to Prevent Blindness, Inc, New York, NY. This study was presented in part as a poster at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Ft Lauderdale, Fla, May 6, 2002.

Corresponding author: Judy E. Kim, MD, Department of Ophthalmology, Medical College of Wisconsin, 925 N 87th St, Milwaukee, WI 53226 (e-mail: judykim@mcw.edu).


Correction

Author’s Name Misspelled. In the article titled “Pathogenesis of the Vitreous Cloud Emanating From Subretinal Hemorrhage,” published in the January issue of the ARCHIVES (2003;121:91-96), Dr Steven McCormick’s name was misspelled in the byline and the affiliation footnote on page 91. The journal regrets the error.