

Penetration of Antifungal Medication

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Keratomycosis and fungal endophthalmitis are extraordinarily difficult from a therapeutic standpoint, both because of the limited number of antifungal agents available for treatment of such problems, and because of the notoriously poor penetration of most antifungals into the cornea, much less into the anterior chamber and vitreous.

We studied, more than nearly two decades ago, the intraocular penetration of the then relatively new imidazole, Miconazole, after topical application. We used the 1% intravenous solution (10 mg/ml) taken directly from the intravenous bottle for topical application, and we studied intraocular penetration after intravenous, subconjunctival, and topical application. We showed that subconjunctival injection was well tolerated, and that penetration into the aqueous humor was exceptionally high after subconjunctival administration of 10 mgs. of the drug. Intravenous administration resulted in high levels of the drug briefly (2 hours), with rapid decay of detectable drug thereafter. Corneal levels were also exceptionally high after subconjunctival administration of the medication, particularly in the presence of an epithelial defect.

Not surprisingly, intraocular levels after topical administration were unimpressive in the presence of an intact epithelium, but quite respectable in the presence of an epithelial defect. Corneal levels were exceptionally high when an epithelial defect was present, and moderate with an intact epithelium. These studies indicated that miconazole penetrates into the cornea and into the aqueous humor after topical, subconjunctival, and even intravenous administration. The highest and most sustained levels occurred after subconjunctival injection, particularly in the context of an epithelial defect.

Our additional studies on the imidazoles disclosed that the oral administration of ketoconazole, 400 mgs. a day, also results in high intraocular and corneal levels of this broad spectrum antifungal drug. The same is true of 5-flucytocine and of fluconazole, of ketoconazole, and econazole. The polyenes, amphotericin-B and Natamycin, penetrate quite poorly, in striking contrast to the imidazoles. However, because of the relatively extensive clinical experience with the latter, polyenes still remain a mainstay of therapy of both corneal and intraocular fungal infections. Regrettably, data exists which would suggest antagonism between the polyenes and the imidazoles, and therefore one would consider combination polyene and imidazole therapy with great caution.