



Fungal Keratitis: Looking for New Antifungal Agents

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Introduction

Fungal keratitis is an important ophthalmic problem all over the world, because it leads to corneal blindness and sometimes loss of the eye. Its outcome depends ultimately on the interplay of the agent (virulence, resistance to drugs, and toxicity) and host factors (predisposing factors such as diabetes, immunosuppression and chronic ocular surface disease) in addition to timely diagnosis and appropriate medical treatment.

Persistent epithelial defect and suture related problems have been found to be the major risk factors predisposing to postkeratoplasty microbial keratitis. The infection of the corneal graft is one of the most serious complications following keratoplasty, and studies have reported that most graft infections usually occur within 1 year of corneal transplantation [1].

Candida albicans is the most frequent cause of fungal keratitis in temperate regions, is an opportunist that can complicate chronic keratopathy and corneal grafts, often misdiagnosed, and despite antifungal therapy, sometimes lead to loss of the eye or poor visual outcome [2,3]. Progressive keratomycosis may lead to keratoplasty in up to one-third [4], and an infected corneal transplant portends regrafting (infectious keratitis following corneal transplantation is one of the leading causes of failure of a corneal graft).

Nowadays, there is no agreed protocol for the treatment of suspected fungal keratitis.

The mainstay therapy is topical amphotericin B (AMB), with an oral azole for severe infection. Voriconazole has

been reported to be effective in the treatment of fungal keratitis because it's broad spectrum coverage and good intraocular penetration following oral administration [5,6]. However, there have been some reports of fungal keratitis cases that did not respond to these treatments [7].

In these cases, new antifungal agents offer promising alternatives: Caspofungin (CAS) is a first-in-class echinocandin with potent activity against *Candida* and *Aspergillus*, the dominant human fungal pathogens. In contrast to all other antifungal drugs (that target the cell membrane), echinocandins act on the fungal cell wall by inhibiting the synthesis of an essential component, the [1,3]-D-glucan. In vitro and in vivo CAS is fungicidal against all *Candida* sp, including fluconazole-resistant strains. Its activity differs from the azole antifungal group that is fungostatic for *Candida* sp. So, voriconazol can stop progression of the infiltrate, but did not kill the microorganism. The presence of the fungus after months of treatment in some cases could be due to poor penetration of drug, resistance of fungus to drugs, or both. An ideal treatment protocol should include antifungal agents chosen by in vitro susceptibility of the fungus, the duration of which should be assessed by in vivo monitoring of fungal filaments or yeasts.

Randomized clinical trials with CAS in patients with candidemia, invasive candidiasis, and *Candida* esophagitis demonstrate that its efficacy is equivalent to that of AMB, with substantially fewer toxic effects [8]. Other echinocandins such as micafungin have been used to treat

ocular fungal infections [9]. However, future studies with larger sample sizes may be called for, to further evaluate its efficacy and tolerance.

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