
IN VITRO INTERACTION OF POSACONAZOLE (POS) AND CASPOFUNGIN (CSP) AGAINST CANDIDA GLABRATA

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Objectives: *Candida glabrata* has emerged as a significant systemic pathogen in recent years and oral infections are being reported. Resistance to therapy with fluconazole is common. Posaconazole, a triazole, has been shown to have a broad spectrum antifungal activity and inhibits ergosterol synthesis affecting the integrity of the fungal cell membrane. Caspofungin, an echinocandin, inhibits fungal cell wall synthesis. With differing mechanisms of action, these medications could be effective in combination. The aim of this study was to compare the antifungal susceptibility patterns of *C. glabrata* against combinations of caspofungin and posaconazole. We evaluated the hypothesis that caspofungin and posaconazole combined may be a suitable alternative in treating candidiasis in those patients whose infections are due to *C. glabrata* and have developed resistance to fluconazole.

Methods: Isolates were obtained from the oral cavities of 22 patients with varying causes of immunosuppression. The identities of 119 oral *C. glabrata* isolates were established by plating on chromogenic agar and confirmed with API 20C testing. The isolates were subcultured to ensure purity. *In vitro* interaction against *C. glabrata* was assessed by the Fungus Testing Laboratory at the University of Texas Health Science Center at San Antonio using checkerboard testing with microdilution parameters outlined in NCCLS document M27-A2. Drug interactions were synergistic, additive, or indifferent based on the fractional inhibitory concentration (FIC) index. **Results:** Synergy, defined as $FIC \leq 0.5$, was observed in 4% of the POS-CSP interactions at 24h post-inoculation, and in 18% at 48h. Additive, defined as $0.5 < FIC \leq 1.0$, was observed in 40% of the interactions at 24h, and 72% at 48h. Indifferent, defined as $1 < FIC < 2.0$, was observed in 56% of the interactions at 24h, and 10% at 48h. No antagonism was observed. **Conclusions:** In general, *in vitro* combinations of POS+CSP appeared more efficacious against *C. glabrata* than either drug alone at 48h. Further study should be conducted to evaluate this combination in an animal model.