Examination of the in vitro activity of posaconazole against clinically relevant Candida species with different methods, including time-kill curves

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Summary

Due to the well-known risk factors (cancer, organ transplantation, low or high age, surgical interventions, etc.) the frequency of invasive infections caused by yeasts and moulds has been increased during the past three decades. Different *Candida* species, *Cryptococcus neoformans* and *Aspergillus* species are responsible for 80-90 % of the infections.

At the beginnings of the 1990's the triazoles, then later the echinocandins were introduced into the clinical therapy, which brought a breakthrough in the treatment of invasive fungal infections associated with high mortality.

In my PhD thesis I examined the *in vitro* efficacy of the newest triazole, posaconazole with different methods, in case of the ten most frequent *Candida* species, which were isolated from more than 200 clinical samples in the Department of Medical Microbiology in the University of Debrecen.

Based on my results the posaconazole MIC_{90} values with the broth microdilution method (BMI) (solvent dimethyl sulfoxide) were ≤1 mg/L in the case of all the investigated species. The agreement within ± 1 dilution degree was 86-100 % with the alternative standard microdilution method where we used polyethylene glycol instead of dimethyl sulfoxide for the solubilization of posaconazole. The posaconazole Etest MIC values read after 24 hours showed good (76-98 %) correlation with the standard BMI data.

I also investigated the *in vitro* killing ability of posaconazole by means of determining the minimum fungicidal concentration (MFC) and time kill curves. The time kill curves confirmed the MFC data, that is posaconazole has a fungicidal effect in the case of *Candida inconspicua, Candida lusitaniae, Candida krusei, Candida kefyr*, while it has fungistatic

effect in the case of *Candida albicans, Candida glabrata, Candida tropicalis, Candida guilliermondii.* Although the MFC values were ≤2 mg/L in 71 % of the *Candida parapsilosis* strains, the time kill curves unequivocally showed only fungistatic effect.

In conclusion, posaconazole shows excellent *in vitro* efficacy against *Candida* species as well. It can provide a good therapeutic option against *Candida krusei, Candida inconspicua, Candida lusitaniae* species, which show decreased susceptibility against several antifungal agents. The development of the intravenous formula of this antifungal agent is desirable in the future.

Keywords: posaconazole, Candida, MIC and MFC, fungicidal, time-kill curves
Kulcsszavak: posakonazol, Candida, MIC és MFC, fungicid, idő-ölés görbék