The paradoxical growth of *Candida albicans*, *C. dubliniensis*, *C. krusei* and *C. tropicalis* strains in the presence of high concentration caspofungin

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SUMMARY

Caspofungin, which is a member of the echinocandin antifungal class, is a new antifungal drug that can be used to treat both oropharyngeal and systemic *Candida* infections. During the *in vitro* susceptibility testing many researchers detected growth in higher echinocandin concentrations (Eagle effect), but the exact frequency of the occurrence of this phenomenon was not known.

During our research we examined the paradoxical growth that appears when using large dosage of caspofungin in case of *Candida* species which are important from oropharyngeal point of view (*C. albicans*, *C. dubliniensis*, *C. krusei* and *C. tropicalis*). We also examined this phenomenon through establishing the minimal inhibitory concentration and also with the help of the killing triggered by caspofungin using minimal fungicidal concentration and time-kill curves in two media (RPMI-1640, AM3).

In AM3 the minimal inhibitory concentration results were lower and the trailing effect, which usually perplexed the exact readings, was not present for any of the four species. With the help of minimal fungicidal concentrations and time-kill curves we undoubtedly proved that for *C. tropicalis* the paradoxical growth, like reduced killing ability can be observed in high caspofungin concentrations, regardless of the media. We observed fungistatic effect for *C. albicans* and *C. dubliniensis* isolates in RPMI-1640 but the killing effect was increased after 24h and more so after 48h in AM3 which appeared in the form of paradoxical growth and fungicidal effect. The time-kill curves proved that for *C. krusei* paradoxical growth does not take place in either media.

In our work, we used minimal fungicidal concentration and time-kill curves for the first time to study paradoxical growth. Our results decisively confirmed and refined the result found by other researchers with regards to paradoxical growth. In order to achieve safe echinocandin therapy, preclinical and clinical studies need to be carried out to clarify the *in vivo* significance of the *in vitro* paradoxical growth at high caspofungin concentrations.

Key words: caspofungin, time-kill, paradoxical growth

Kulcsszavak: caspofungin, idő-ölés görbék, paradox növekedés