

P976

Abstract (poster session)

Evaluation of gradient concentration strips for in vitro combination testing of antifungal combinations against *Candida* spp.

M. Siopi*, A. Elefanti, N. Siafakas, L. Zerva, J. Meletiadis (Athens, GR)

Objectives: Antifungal combination therapy may be used to treat refractory fungal infections by *Candida* spp. However, there are challenges associated with the performance of in vitro combination testing in the routine laboratory practice since the microdilution checkerboard method is laborious and time consuming. The aim of our study was to assess the performance of gradient concentration strips versus standard checkerboard method for in vitro testing of antifungal combinations against *Candida* spp. **Methods:** A total of 5 clinical isolates of *Candida* spp., including 2 reference strains (*C. krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019), 1 *C. albicans*, 1 *C. kefyr* and 1 *C. glabrata* were tested. In vitro susceptibility against amphotericin B (AMB), voriconazole (VOR) and caspofungin (CAS) and the two drug combinations AMB+VOR and VOR+ CAS were tested in replicates with a broth microdilution checkerboard test (CHECK) based on EUCAST methodology and the gradient concentration strip (crossing method) according to the manufacturer's instructions for Liofilchem® MIC Test strips (MTS). In vitro combinations were assessed after 24h of incubation based on the fractional inhibitory concentration (FIC) index calculated as $MICAB/MICA+MICBA/MICB$ where MICA and MICB are the minimal inhibitory concentrations (MIC) of drugs alone and MICAB are the MIC of drug A in presence of drug B and vice versa for MICBA. Synergy, additivity and antagonism was defined when FIC indices were ≤ 0.5 , $>0.5- <4$ and ≥ 4 , respectively. FIC indices were compared with paired t test after log₂ transformation. **Results:** In vitro median (range) FIC indices with MTS and CHECK methodologies were 1.6 (0.44-16) and 1.5 (0.38-2.5) for AMB+VOR combination and 2.4 (0.84-9) and 0.63 (0.25-2.13) for VOR+CAS combination, respectively for all isolates ($p > 0.05$). MTS resulted in median (range) 0.42(-0.77-2.41) fold lower FIC indices for AMB+VOR combinations and 1.61 (-0.25-5.17)-fold higher for VOR+CAS combinations compared to CHECK. 45% of FIC indices demonstrated >1-twofold differences. Antagonism was more often observed with MTS method and synergy was more often found with EUCAST method. **Conclusion:** The gradient concentration method was more expensive but less laborious and time consuming than microdilution checkerboard test and resulted in broader FIC ranges. Further optimization of gradient concentration method is required in order to obtain better correlation with reference methodology.