FLUCONAZOLE HETERORESISTANCE IN *CANDIDA PARAPSILOSIS*

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Background: We experience a case of blood stream infection due to *C. parapsilosis* in a patient following cardiac surgery. Here we describe the characteristics of serial isolates of *C. parapsilosis* demonstrated increasing resistance to fluconazole in vitro.
Methods: The five isolates of *C. parapsilosis* were obtained from a patient operated on mitral valve. Antifungal susceptibility was determined by NCCLS microdilution method and E test. Strain identity was determined by pulse field gel electrophoresis. Population analysis was performed to determine whether the phenotype switch is a clonal event or associated with substrain selection. Fluconazole resistant isolates were subcultured in medium without fluconazole to examine stability.

Results: The initial isolate(CP1) was fluconazole susceptible(MIC 2 µg/ml), however, the isolates(CP2 – CP5) developed resistance after a brief usage of fluconazole. DNA typing revealed development of resistance in a persistent strain. On population analysis, CP1 formed colonies on plates containing 64 µg/ml fluconazole at frequencies of 10^{-4}. Clinical isolates CP2, 5 and resistant subclone derived from CP1 demonstrated a homogenous population of resistant cells on plates containing 64 µg/ml fluconazole. The induced resistance was reversible through serial transfers in fluconazole-free media over a period of 30 days.

Conclusions: Fluconazole-heteroresistant phenotype of *C. parapsilosis* was observed in blood stream isolates from a cardiac surgery patient. Fluconazole resistance can be developed by a selection from heteroresistant clones by exposure to fluconazole.