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Fluconazole versus echinocandins in treatment of invasive candidiasis: a nationwide, population-based study in Taiwan

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Background: Invasive candidiasis (IC) is an important healthcare-related infection, with increasing incidence and a crude mortality around 50%. Echinocandins are a safe and candida-cidal agent and active against biofilm. A patient-level quantitative review of randomized trials for treatment of IC showed use of an echinocandin was associated with improved survival and greater clinical success. However, whether echinocandin therapy versus fluconazole results in better outcomes in clinical practice is uncertain.

Material/methods: We conducted a retrospective review of Taiwan National Health Insurance Research Database from 2007 through 2013 for treatment of IC (with one of the following diagnosis at discharge according to ICD-9-CM codes 112.4, 112.5, 112.81, 112.83, and 112.85) and to compare the impact of systemic use for 5 days or longer of echinocandin versus fluconazole on clinical outcomes. Patients with IC during 2007 were excluded. Patients diagnosed with IC and received systemic fluconazole or echinocandins (caspofungin, micafungin, or anidulafungin) monotherapy during January 1, 2008 to December 31, 2012 were identified and compared for length of hospitalization, ICU stay, in-hospital and 1-year all-cause mortality. Cox regression and propensity score matched analyses were performed. Comorbidities were those coded in the preceding 6 months of the index date, that is, the date of admission of the first hospitalization. Continuous variables were analyzed using Mann-Whitney U test; categorical variables were analyzed using chi-square test.

Results: A total of 694 patients with IC were identified during the study period. The incidence of IC per 100,000 population increased from 1.15 cases in 2008 to 2.42 cases in 2012. Of them, 84.73% were treated with only one antifungal agent including 143 echinocandin-treated patients and 386

fluconazole-treated patients. Higher proportions of patients in the echinocandin group had neoplasm of lymphatic and hematopoietic tissue, renal disease, diabetes, and systemic antifungal therapy for infections other than IC in 1 month prior to index hospitalization than the fluconazole group. Median length of hospital stay was 38.5 days for echinocandins group and 32 days for fluconazole group ($p=0.003$). The percentage of patients required ICU care was 51.8% and 46.4% in echinocandin and fluconazole group, respectively ($p=0.27$). Median length of ICU stay was 17 days with fluconazole and 19 days with echinocandins ($p=0.26$). In-hospital mortality was 29.5% with fluconazole and 37.1% with echinocandins ($p=0.10$). Multivariate cox regression analysis showed that the median length of hospital stay was 9.04 days longer with echinocandins than fluconazole (95% confidence interval [CI] 1.44-16.64, $p=0.019$). Use of echinocandins for IC was not associated with lower in-hospital mortality (adjusted relative risk 1.32, 95% CI 1-1.74, $p=0.055$) or 1-year mortality (adjusted relative risk 1.04, 95% CI 0.91-1.2, $p=0.58$).

Conclusions: The use of an echinocandin for patients with IC in Taiwan was not associated with shorter hospital stay or lower in-hospital mortality.