Antifungal Prophylaxis in Liver Transplant Recipients

TO THE EDITOR—We read with interest the article by Saliba and colleagues reporting the results of the TENPIN (Liver Transplant European Study Into the Prevention of Fungal Infection) trial comparing micafungin with standard care for antifungal prophylaxis in liver transplant recipients [1]. We wish to make several comments related to the trial.

Three different agents (fluconazole, liposomal amphotericin B, or caspofungin) were used for standard care. Thus, it would be helpful for the authors to provide the number of patients receiving each agent and give a comparison of the clinical success rate for micafungin with each standard prophylactic agent as described in their Table 2. Furthermore, as the study was designed primarily to demonstrate noninferiority of micafungin to standard care for antifungal prophylaxis, the results of the study, for the most part, were predictable. A previous prophylactic study in high-risk liver transplant recipients found that micafungin was as efficacious as a lipid complex formulation of amphotericin B, with less renal toxicity [2]. In the TENPIN study, the only significant difference in toxicity between micafungin and standard care was less renal toxicity compared to liposomal amphotericin B. Based on current knowledge of the echinocandins, it would be very unlikely for micafungin to be inferior to caspofungin for antifungal prophylaxis. On the other hand, echinocandins have activity for fluconazole-resistant Candida species as well as Aspergillus. Nonetheless, in the appendix of this article, invasive fungal infections (IFIs) due to Candida or Aspergillus occurred in 7 micafungin patients and in 4 fluconazole patients. Thus, there would appear to be no significant differences in the overall effectiveness of micafungin and fluconazole in the TENPIN trial. The possible advantages of micafungin and other echinocandins over fluconazole (lack of harmful drug interactions, greater effectiveness in dialysis patients) mentioned in the authors’ discussion do not appear to be supported by any data from their study.

Since our initial placebo-controlled trial demonstrating the efficacy and safety of fluconazole for prevention of IFI in liver transplant recipients [3], and based on Infectious Diseases Society of America and American Society of Transplantation guidelines [4, 5], we have primarily used fluconazole for antifungal prophylaxis in high-risk liver transplant recipients. However, like Saliba and colleagues, we also performed a multicenter, randomized, double-blind trial comparing the efficacy and safety of an echinocandin (anidulafungin) with fluconazole for antifungal prophylaxis in high-risk liver transplant recipients. We wish to make several comments related to the trial.

Recent studies have found that a MELD score ≥30 may be the most influential factor for IFI in the MELD era of liver transplantation [7, 8]. Despite the greater acuity of the patients in our study, the incidence of IFI was similar with fluconazole prophylaxis (8.0%) and anidulafungin prophylaxis (5.1%). There was no toxicity with either drug. Graft rejection, fungal-free survival, and mortality were similar in both study groups. The TENPIN trial also shows that standard prophylaxis is as effective as micafungin prophylaxis. In our trial, anidulafungin prophylaxis was associated with a trend toward less Aspergillus colonization or infection and fewer breakthrough IFIs among patients who had received pretransplant fluconazole.

A transplant center should adopt an antifungal prophylactic strategy based on risk factors for IFI in their patients, the sensitivity profile of local fungal pathogens, and drug costs. At the University of California, Los Angeles Medical Center, where the median MELD score of transplant recipients is 36 and >60% of all liver transplant patients have a MELD score ≥30, we continue to use fluconazole as the primary agent for antifungal prophylaxis in high-risk patients. To avoid the overuse of more expensive echinocandins and to prevent potential increased echinocandin resistance, we reserve an echinocandin for patients who have an increased risk for invasive aspergillosis or develop an IFI resistant to fluconazole [9]. Using this approach, we have found that <10% of our patients need an echinocandin and rarely experience a fatal IFI.

Notes

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