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LETTER TO THE EDITOR

The issue of the antifungal drug choice in prophylaxis of invasive fungal infection after liver transplant

To the Editor,

We read with interest the study by Jorgenson et al[1] concerning the implementation of a targeted Fungal Prophylaxis Protocol (FPP) in the immediate post-operative liver transplant (LT). They used a static dosing of fluconazole 400 mg a day over 14 days in patients with high-risk criteria. This approach significantly reduced invasive fungal infection (IFI) after LT, did not adversely affect their fungal epidemiology, and could have a positive impact on allograft and patient survival.

However, in the study, the majority of IFI were *Candida* species, and after the implementation of the protocol, only *Candida* species were isolated, while *Aspergillus* did not account for any IFI in both historical and implemented group. These findings are very attractive but quite uncommon. Indeed, if *Candida* infections are the most frequent IFI, severe IFI due to *Aspergillus* or other molds can also occur, mainly in post-LT patients with acute renal failure associated with severe liver failure or massive blood transfusion.[2,3] Although a systematic review and network meta-analysis by Evans et al[3] reported an equivalent efficacy of fluconazole compared to liposomal amphotericin B (as well as the non-inferiority of echinocandins compared to fluconazole), the inefficacy of fluconazole on mold infection can be dangerous for some high-risk patients. In fact, the kind of IFI also depends on other incidental factors such as geography and the place where patients live (countryside or city), their employment and even the medical facility (a new or an old building). The colonization by mold spores in the upper respiratory airways relies mostly on these factors and the occurence of post-operative complications (acute renal failure, bleeding, delayed graft function, sepsis) can facilitate the development of *Aspergillus* infection.

So the choice of antifungal drug prophylaxis should be made on the basis of the local epidemiology of IFI observed in each center. This could explain why in the study by Jorgenson[1] the implementation of targeted FPP with fluconazole reduced significantly IFI and it resulted in a protective effect against IFI, while in the study by Giannella et al[4] prophylaxis with fluconazole was an independent risk factor for IFI. In our experience,[5] the majority of IFI are *Aspergillus* pulmonary infections and in some very complex patients the mold infection was diagnosed as soon as the first day after LT. Hence, the use of a prophylaxis with anti-mold activity in the immediate post-LT period is of paramount importance in our center.

Although we do agree that a simplified prophylaxis protocol increases compliance and consequently reduces IFI, we still believe that an approach based on a diversification of risk factors for *Candida* or mold infection and local epidemiological data would better allow for a tailored prophylaxis using different antifungal drugs with or without anti-mold activity.

KEYWORDS

antifungal prophylaxis, invasive fungal infection, liver transplant recipients

CONFLICT OF INTEREST

None of the authors have a disclosure related to this study to declare.

AUTHOR CONTRIBUTIONS

All authors contributed to the drafting of this manuscript. BL and FGDR participated in research design and in the writing of the paper. RR and RB participated in the writing of the paper. RR and FGDR reviewed the manuscript.

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