Bruno Viaggi
Carlo Tascini
Francesco Menichetti

Acid-suppressant therapy does not influence absorption of azoles used in candidemia

Accepted: 6 February 2015
Published online: 21 February 2015
© Springer-Verlag Berlin Heidelberg and ESICM 2015

Dear Editor,
Daniell [1] in his letter outlined the possibility that the effective blood concentration of orally administered antifungal drugs might be reduced by concomitant administration of acid-suppressant therapy (AST). In fact therapeutic drug monitoring of orally administered posaconazole showed high variability in blood levels, especially when co-administered with AST.

This in fact may be relevant for the setting of patients with haematological malignancies receiving antifungal prophylaxis mainly directed against mould infections (*Aspergillus* spp., *Mucor*). Though it is true that AST, by increasing gastric pH, may limit the acid-dependent transformation of these relatively insoluble compounds into their soluble derivatives, another aspect is more relevant here: AST is proven to interact with the absorption of less soluble molecules such as posaconazole, itraconazole and ketoconazole

but not with the absorption of more soluble molecules such as voriconazole or fluconazole.

Because a “timely” and adequate antifungal therapy decreases the mortality rate, the goal of an oral therapy is to reach a therapeutical blood level.

The use of an oral antifungal therapy with an azole (namely fluconazole) is no longer recommended as a starting treatment for a life-threatening disease such as candidemia. However, a de-escalation therapy with fluconazole (also an oral formulation) may be useful in order to reduce the length of stay.

Many authors who have studied the mortality related to the onset of an adequate antifungal therapy did not describe the molecules used. They have, however, studied patients treated only with intravenously administered drugs such as caspofungin [2].

On the other hand, Bassetti et al. [3] found that 40 % of patients with candida septic shock were treated with azoles, but only fluconazole was used. Again, Grim et al. [4] found that 40 % of patients were treated only with fluconazole (177 patients). Finally, Garey et al. [5] studied, by definition, only patients treated with fluconazole.

No study was found in which other lipid-soluble azoles (namely posaconazole, itraconazole or ketoconazole) were used as first-line or de-escalation therapy for candidemia.

Therefore, although the observation by Daniell is timely and useful, in our opinion it is not adequate for patients with candidemia. It is more relevant for haematological patients

that are often treated with these lipophilic azoles.

References

1. Daniell HW (2015) Inhibition of antifungal therapy by gastric acid suppressants. *Intensive Care Med*. doi:10.1007/s00134-015-3673-9
2. Hsu DI, Nguyen M, Nguyen L, Law A, Wong-Bernger A (2010) A multicentre study to evaluate the impact of timing of caspofungin administration on outcomes of invasive candidiasis in non-immunocompromised adult patients. *J Antimicrob Chemother* 65:1765–1770
3. Bassetti M, Righi E, Ansaldi F, Merelli M, Cecilia T, De Pascale G, Diaz-Martin A, Luzzati R, Rosin C, Lagunes L, Trecarichi EM, Sanguinetti M, Posteraro B, Garnacho-Montero J, Sartor A, Rello J, Rocca GD, Antonelli M, Tumbarello M (2014) A multicenter study of septic shock due to candidemia: outcomes and predictors of mortality. *Intensive Care Med*. doi:10.1007/s00134-014-3310-z
4. Grim SA, Berger K, Teng C, Gupta S, Layden JE, Janda WM, Clark NM (2012) Timing of susceptibility-based antifungal drug administration in patients with *Candida* bloodstream infection: correlation with outcomes. *J Antimicrob Chemother* 67:707–714
5. Garey KW, Rege M, Pai MP, Mingo DE, Suda KJ, Turpin RS, Bearden DT (2006) Time to initiation of fluconazole therapy impacts mortality in patients with candidemia: a multi-institutional study. *Clin Infect Dis* 43:25–31

B. Viaggi (✉)
Neurointensive Care Unit, AOU Careggi
Firenze, Florence, Italy
e-mail: bruno.viaggi@gmail.com

C. Tascini · F. Menichetti
Infectious Diseases Unit, Nuovo Santa
Chiara Hospital, Pisa, Italy