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LETTER TO THE EDITOR

Antifungal Stewardship in Light of the Updated Evidence on Untargeted Antifungal Treatment in Critically Ill Patients

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To the Editor,

We read with great interest the article by Andruszko et al. [1] describing the primary goals of an antifungal stewardship program, methods for its implementation, and potential benefits in terms of better utilization of resources and outcomes.

We agree with the authors on the lower number of reported experiences of antifungal stewardship programs compared to antibacterial initiatives, and we appreciated the efforts to highlight the complexity of an antifungal stewardship program in terms of patient selection, early institution of effective antifungal treatment, implementation of methods for early diagnosis of invasive fungal infections, outcome monitoring, promotion of audits, and educational interventions.

The issue of early institution of effective antifungal therapy is pivotal to improve patient outcome, and authors reported different approaches for early antifungal administration in selected patients. Since widespread use of antifungals in patients without clear fungal infections may have drawbacks in terms of higher costs and increasing antifungal resistance, strong evidence should justify this approach. Authors reported results of meta-analyses published nearly 10 years ago investigating the administration of antifungals as prophylaxis in surgical patients only, showing a reduction of candidemia without a benefit in terms of mortality. However, our group provided an update of this evidence. Indeed, we recently published a Cochrane systematic review investigating the use of antifungals as untargeted treatment in non-neutropenic critically ill patients, namely the administration of antifungal agents before definitive diagnosis of fungal infections [2]. We included studies investigating the prophylactic, pre-emptive, and empiric approaches. Our meta-analysis, including 22 randomized trials involving 2761 patients, showed a reduction of invasive fungal infections when antifungals were given as an untargeted treatment despite the absence of benefit in terms of mortality [2]. Notably, the lack of a survival benefit was reported irrespective of the molecular drug used or the type of untargeted approach [3]. This paradox may be explained, at least in part, by the improved overall patient care of critically ill patients during the last decade which may have diluted the survival benefit of antifungal administration originally observed in older studies and, in some studies, by the enrolment of patients in a too-late phase of fungal infection process [4]. Another explanation may rely on the impaired immune response recently observed in non-neutropenic critically ill patients [5].

Among the different untargeted strategies, the pre-emptive approach has been investigated only by one randomized trial to date [6]. Recently, Posteraro et al. [7], in a retrospective study, investigated the combination of Candida score and (1–3)-β-d-glucan (BDG) assay for selection of high-risk patients who would have benefitted from antifungal administration. This strategy led to reduction of antifungal administration to 73 % of patients with negative BDG results and to shortened treatment duration in another 20 % of patients [7]. Indeed, both clinicians and researchers should balance the benefit of early antifungal administration to the risk of selection of antifungal drug resistance which has been reported even for the recently introduced echinocandins. If confirmed in a randomized trial, these results would lead to a more effective patient selection and would enhance the adoption of an antifungal stewardship program [8].

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References

1. Andruszko B, Ashley E. Antifungal stewardship: an emerging practice in antimicrobial stewardship. Curr Clin Micro Rpt. 2016;3:111–9.
2. Cortegiani A, Russotto V, Maggiore A, Attanasio M, Naro AR, Raineri SM, et al. Antifungal agents for preventing fungal infections in non-neutropenic critically ill patients. Cochr Data Syst Rev. 2016;1:CD004920.
3. Cortegiani A, Russotto V, Raineri SM, Giarratano A. Antifungal prophylaxis: update on an old strategy. Eur J Clin Microbiol Infect Dis: Off Publ Eur Soc Clin Microbiol. 2016.
4. Cortegiani A, Russotto V, Raineri SM, Giarratano A. The paradox of the evidence about invasive fungal infection prevention. Crit Care (London, England). 2016;20(1):114.
5. Russotto V, Cortegiani A, Raineri SM, Giarratano A. From bedside to bench: the missing brick for patients with fungal sepsis. Crit Care (London, England). 2016;20(1):191.
6. Namikawa T, Kitagawa H, Yamatsuji T, Naomoto Y, Kobayashi M, Hanazaki K. Pre-emptive treatment of fungal infection based on plasma β-D-glucan levels after gastric surgery for gastric cancer in elderly patients. J Gastroenterol Hepatol. 2013;28(9):1457–61.
7. Posteraro B, Tumbarello M, De Pascale G, Liberto E, Vallecoccia MS, De Carolis E, et al. (1,3)-Beta-d-glucan-based antifungal treatment in critically ill adults at high risk of candidaemia: an observational study. J Antimicrob Chemother. 2016;71(8):2262–9.
8. Cortegiani A, Russotto V, Raineri SM, Giarratano A. Is it time to combine untargeted antifungal strategies to reach the goal of 'early' effective treatment? Crit Care (London, England). 2016;20(1):241.