Candida species may cause both superficial and invasive infections. Invasive fungal infections and candidemia may lead to disseminated disease and are associated with high mortality [1]. Even positive cultures of Candida species from central venous catheters have been associated with high mortality and should be treated with antifungal agents [2]. Over time, the epidemiology of Candida infections has changed. The incidence of candidemia has dropped, but the number of Candida bloodstream infections (BSI) due to Candida glabrata has increased markedly. Over a decade the occurrence of candidemia due to a non-albicans species has doubled [3]. This fact has implications for pharmacotherapy. In the Netherlands candidemia patients have a 50% chance of having Candida non-albicans species [4]. The most important pathogens among the non-albicans species are C. glabrata and C. parapsilosis. As around 10-30% of Candida glabrata are resistant to the most commonly-used fluconazole, recent national guidelines no longer advocate fluconazole as first line of treatment in BSIs caused by unknown Candida species [5]. Although C. krusei is intrinsically resistant to fluconazole, infections are rare (<1%) and therefore rarely have to be considered in selection of antifungal agents. C. parapsilosis is possibly less susceptible to echinocandins.

Echinocandins are antifungal drugs that inhibit the synthesis of glucan in the cell wall, probably via non-competitive inhibition of the enzyme 1,3-β-glucan synthase, and may be regarded as the penicillin of antifungal agents [6-7]. In this issue of the Netherlands Journal of Critical Care, Rotstein and coworkers have reviewed the literature on echinocandins [8]. Both the authors and national guidelines have changed the secondary position of echinocandins in the treatment of invasive fungal infections into the first line treatment [5]. In other words, echinocandins are now in the driver’s seat and may be considered first choice for invasive Candida infections in non-neutropenic critically ill patients. Thus, in general, initial therapy will be commenced using echinocandins and in cases of C. albicans or C. parapsilosis, treatment may be switched to fluconazole. However, there is some evidence that even continuation of echinocandins in C albicans infections may be superior to fluconazole [9]. It is not unlikely that in the future guidelines will advise the institution of a complete course of echinocandins in invasive C albicans infections. At present more data are warranted as echinocandins incur more costs and evidence for their superiority in treating C albicans infections is scarce.

Of the echinocandins already available, anidulafungin (Ecalta®, Pfizer) and caspofungin (Cancidas®, MSD) are well known. Both these echinocandins are more expensive than fluconazole. Therefore it is important to know that in the Netherlands hospitals can be reimbursed for up to a maximum of 80% of the drug acquisition costs of these echinocandins, in accordance with national regulations on expensive medications (NZa Beleidsregel CI-1135). Recently a third echinocandin micafungin (Mycamine®, Astellas Pharma) which is frequently prescribed worldwide, has become available in the Netherlands. It should be taken into account that although up to 80% of the cost of echinocandins may be reimbursed it remains a major cost for the Dutch healthcare system. Therefore it could be important to know when it would be safe to start fluconazole without the risk of using fluconazole in infections with Candida species not susceptible to the drug.

Recently Cohen and coworkers published data concerning the early prediction of Candida glabrata fungaemia in non-neutropenic critically ill patients. They found six independent risk factors for Candida glabrata fungaemia: age > 60 years (Odds Ratio (OR) 4.7), recent use of cephalosporins (OR 4.5), solid tumor (OR 6.0), and the absence of diabetes mellitus (diabetes mellitus OR 0.1) [10]. These data may help to select patients at high-risk for Candida glabrata infections.

In the near future new detection methods will speed up the diagnostic work-up and potentially lead to better targeting of echinocandins and the reduction of the number of treatment days on echinocandins in fluconazole-susceptible Candida species. Invasive Candida infections can be diagnosed using conventional approaches (microscopy, culture, serology), as well as new methods including antigen detection and polymerase chain reaction (PCR) assays. Antigen detection and PCR assays represent a valid alternative, in terms of their high potential sensitivity and specificity, but these procedures still need to be standardized and evaluated in a large number of patients [11-12].

Concluding, a new era of pharmacotherapy in invasive Candida infections has come with the availability of echinocandins in the pharmacological armamentarium of the intensivist. We can be confident that this will lead to better outcomes in relevant critically patient groups.
Conflict of interest:
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References