Original Research

Caspofungin Treatment for Pulmonary Invasive Fungal Disease in Hematology Patients: A Retrospective Study in a Clinical Practice Setting in China

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ABSTRACT

Purpose: Invasive fungal disease (IFD) is a serious complication in patients with hematologic malignancies. Caspofungin is the first approved inhibitor of fungal β-1,3-glucan synthesis. The aim of the present study was to evaluate the effectiveness of caspofungin in the treatment of IFD in patients with hematologic malignancies.

Methods: In this retrospective study, data from the electronic medical records of 1118 inpatients who were admitted to 10 hospitals in China between 2013 and 2014 were analyzed. Inclusion criteria were hematologic disorder and IFD diagnosed during the hospitalization, based on clinical manifestations or evidence of pulmonary invasion, as well as caspofungin treatment for at least 7 days. The primary end point was the favorable response rate at the end of caspofungin as initial therapy for proven/probable/possible pulmonary IFD. The secondary end point was the survival rate after the completion of the caspofungin treatments.

Findings: A total of 704 patients were included, of whom 122 had IFD classified as probable/possible and 582 had unclassified IFD. The most frequent hematologic diseases were acute myeloid leukemia (42.8%), followed by acute lymphatic leukemia (18.8%), non-Hodgkin lymphoma (8.8%), aplastic anemia (7.1%), and others (22.5%). The rates of favorable caspofungin response were 57.2% in all patients, 58.2% in the probable/possible IFD group, and 57.0% in the unclassified IFD group. Caspofungin as initial monotherapy led to a favorable response rate of 62.2% in the probable/possible IFD group. Uni- and multivariate analyses revealed that not recovering from neutropenia during antifungal treatment, and advanced age, were significant factors for unfavorable outcomes. The overall IFD-related mortality rate was 4.1%.

Implications: The results of our study show that caspofungin treatment of IFD in hematology patients was reasonable, with an overall rate of favorable

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response of 57.2% with each caspofungin treatment strategy. (*Clin Ther.* 2017;39:1758–1768)

Key words: caspofungin, echinocandin hematological disorders, invasive fungal infection, lymphatic leukemia.

INTRODUCTION

Invasive fungal disease (IFD) is a major complication in patients with hematologic malignancies. The majority of patients in whom IFD develops acute myeloid leukemia cases or recipients of allogeneic hemopoietic stem cell transplantation,[1] with mortality rates of 13.5% to 28.6%.[2,3]

IFD is mainly caused by *Candida* and *Aspergillus* spp.[4] Improvements in early diagnosis and timely initiation of antifungal treatment play a crucial role in the outcome, because the mortality rates are highly associated with delayed medication.[5–7] Amphotericin B (AmB) formulations have been standard therapy for decades, but they have limited usefulness due to well-known nephrotoxicity and infusion-related toxicity (deoxycholate AmB).[8–10] Lipid formulations of AmB have been proved to be less toxic, although they are not more effective than conventional AmB.[11] However, in 2002 voriconazole was shown to be more efficacious than AmB in the treatment of proven/probable aspergillosis in 277 patients with 86.6% lung infections and mixed immunocompromising conditions.[12] Thus, voriconazole became the first-line therapy for invasive pulmonary aspergillosis, which is reflected in the 2016 guideline from the Infectious Diseases Society of America, which stated that AmB deoxycholate and its lipid derivatives might be considered as alternative medications for invasive pulmonary aspergillosis when voriconazole cannot be administered, or in resource-limited settings when no other agent is available. Lipid formulations of AmB should be the treatment of choice when azoles are contraindicated or not well-tolerated.[13–15]

Caspofungin is an echinocandin that disrupts fungal cell wall integrity by inhibiting fungal 1,3-β-glucan synthase.[16] It has been associated with fewer infusion-related adverse events, is not nephrotoxic, and has not been associated with major drug-to-drug interactions involving cytochrome P450, as are triazole agents with anti-*Aspergillus* activity.[17] Therefore, caspofungin administered as monotherapy or in combination therapy can be considered as an alternative choice in patients who are unable to tolerate azole medications.

Caspofungin is the first fungal (1→3)-β-D-glucan synthesis inhibitor approved by the US Food and Drug Administration that has activity against *Candida* and *Aspergillus* spp and has been shown to be a reasonable primary treatment of candidemia[18] and other forms of invasive candidiasis,[19] as well as salvage therapy for invasive *Aspergillosis* infection.[20] In addition, it is recommended as empirical therapy for presumed fungal infections in febrile neutropenic patients.[21] Caspofungin has been approved in China for about 10 years, but there is a lack of data from clinical practice on caspofungin treatment outcomes in patients in hospitals in China.

In the present investigation, through a multicenter, observational, retrospective study of data from 10 hospitals, we analyzed the curative effectiveness of caspofungin in hematology patients with pulmonary IFD in China, focusing on caspofungin as the initial monotherapy or combination therapy and evaluating its usability in patients unable to tolerate azole medications.

PATIENTS AND METHODS

This study was conducted according to the International Conference on Harmonisation guideline on Good Clinical Practice and the Declaration of Helsinki (2004). The protocol was approved by the ethics committees at the 10 participating study centers. Written informed consent was obtained from all of the patients before their participation in the study. The aim of this multicenter, observational, retrospective analysis was to estimate the curative effects of caspofungin in hematology patients with pulmonary IFD.

Inclusion Criteria

In this study, data from the electronic medical records of 1118 inpatients between 2013 and 2014 who were admitted into 10 hospitals during a predefined period due to hematologic disorders were analyzed. Inclusion criteria for patients in the present study were: (1) age ≥16 years and at least 1 diagnostic criterion (hematologic malignancy [eg, acute leukemia, lymphoma, myelodysplastic syndrome, multiple myeloma], aplastic anemia, or history of hematopoietic stem cell transplantation) during