



The Utilization Pattern of Caspofungin in an Educational Hospital

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ABSTRACT

Background: Caspofungin is prescribed for the systemic treatment of fungal infections and its correct prescription pattern is an issue of importance. Hence in this study Caspofungin utilization and the frequency rate of medication errors were investigated at a training hospital in a developing country.

Methods: This cross-sectional study enrolled 43 consecutive patients receiving Caspofungin in Firoozgar Hospital, Tehran, Iran from March to September 2017.

Results: The prescription frequency was higher in Intensive Care Unit by a rate of 58.1%. Infectious disease specialists were responsible for Caspofungin prescription only in 11 cases (25.5%). The cause of Caspofungin prescription was unknown in 18.6% of cases; but empiric treatment for febrile neutropenia and ICU patients with Candida Score > 2.5 were the most known causes. The drug administration in 11 cases (25.6%) occurred in less than one hour. The indication of treatment was incorrect in 12 out of 43 cases (28%). On the first day of the treatment a dose of both 70 mg and 50 mg was prescribed, which was higher than the appropriate dose and also it was lower than the optimal dose in five cases (83.7%). The mean treatment duration was 10.88 ± 5.35 days ranging from 2 to 24 days. The duration of treatment was correct in 20 cases (46.5%) and incorrect for 23 patients (53.5%).

Conclusion: In comparison with the Sanford and IDSA Guidelines there are multiple discordances in our setting, such as inappropriate duration, continuation, and indications. Hence these should be announced to the physicians for taking further caution in the aforementioned cases, and it is advisable to consult with infectious diseases specialists for the administration of anti-fungal drugs.

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Introduction

Development of a scientific rational drug delivery system in hospitals is crucial (1-3). The evaluation of drug

prescription in hospitals with appropriate rational patterns would result in decreased costs, less medication errors and increased efficiency (4-6). In fact in a hospital the number of drugs, rate of the prescribed antibiotics, and number of

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injection drugs are indicators of correct drug prescription and criteria for assessing physicians' functionality (3). Inappropriate drug use in hospitals is seen in both developed and developing countries (1), which can be monitored and prevented easily by physicians (7-10). Drug utilization evaluation (DUE) in hospitals, especially for the antibiotics and anti-fungal agents in arrangement with an accurate pattern of use, is the initial executive step that can be taught in training hospitals (11). Such studies may focus on the drug or the therapeutic course, drug use, and administration (12, 13).

Antifungal use is a common practice in hospitals for many infectious diseases worldwide but with a higher frequency in developing countries such as Islamic Republic of Iran (14-16). Caspofungin is prescribed for the systemic treatment of fungal infections and its true and correct prescription pattern is an issue of importance (14). Caspofungin is an intravenous antifungal lipoprotein derivative, which is a new echinocandin antifungal agent with an action mechanism that targets a structural component of the fungal cell wall including 1,3-Beta glucan synthase with inhibitory action (14). It may be used to treat Aspergillus, Candidiasis, and Cryptococcus neoformans. The possible side effects include fever, headache, liver enzyme increase, anaphylaxis, phlebitis, tachycardia, paresthesia, and gastrointestinal complaints (15, 16). The main gap detected by the authors of this novel study is that in the previous studies conducted in the Middle East, the efficacy and safety of Caspofungin were investigated but the drug's prescription pattern was rarely evaluated. Hence in this study the main objective is finding a probable answer to the following research questions: 1) What should the correct utilization pattern of Caspofungin be like, and 2) how much is the frequency rate of medication errors at a training hospital in a developing country. The appropriateness of Caspofungin's prescription is assessed based on Sanford and Infectious Disease Society of America (IDSA) Guidelines.

Methods

This cross-sectional study enrolled 43 consecutive patients receiving Caspofungin in Firoozgar Hospital, Tehran, Iran from March to September 2017. All prescriptions either with or without insurance coverage were gathered through examining the patients' archived medical files, using existing medical documents in the hospital's pharmacy. The exclusion criterion was incomplete documents.

The study was approved by local ethical committee at Iran University of Medical Sciences. The prescription frequency of the drug was compared with the data standardized by Iranian Health Ministry in Drug and Food Department and the suggested rates by IDSA and Sanford Guideline. Also the indications for Caspofungin prescription were determined by a revision of existing

medical data. Consequently, reasons as to why Caspofungin was prescribed for every patient at this training hospital were investigated. We determined the appropriateness of Caspofungin use in terms of right indication, right dose, right duration and right monitoring by comparison with Sanford and IDSA Guidelines.

SPSS version 18.0 software was used for data analysis. The categorical data were shown in the form of frequency and percentage. There was no previous work of research compatible to our study, so no P value is presented as this study is merely descriptive. Also the numeric variables were reported as mean and standard deviation.

Results

Among 43 enrolled patients 21 subjects (48.8%) were male. The mean age was 50.1 ± 20.4 years. The underlying diseases of the patients are shown in Table 1.

Table 1. Underlying disease in patients receiving Caspofungin

Underlying disease	Frequency	Percent
Pneumonia	8	18.6%
Non-hematological malignancy	9	20.9%
Intra Cerebral Hemorrhage	5	11.6%
Hematological malignancy	3	6.9%
CerebroVascular Accident	3	6.9%
Intra-abdominal infections	3	6.9%
Wound Infection	3	6.9%
Chronic renal failure	2	4.6%
Adhesion band obstruction	2	4.6%
Acute gastrointestinal bleeding	2	4.6%
Hepatic failure	1	2.3%
Inflammatory Bowel Disease	1	2.3%
Guillain-Barré syndrome	1	2.3%

The prescription rates across the wards are shown in Table 2. Infectious disease specialists were responsible for Caspofungin prescription in only 11 cases (25.5%). The reasons of Caspofungin prescription are shown in Table 3. Empiric treatment for febrile neutropenia and Intensive

Care Unit (ICU) patients with Candida Score > 2.5 were the most reasons of Caspofungin prescription.

Table 2. Admission ward in patients receiving Caspofungin.

Ward	Frequency	Percent
Internal ICU	12	27.9%
Surgical ICU	7	16.2%
Hematology - Oncology	6	14%
Neurology ICU	4	9.3%
Gastroenterology	3	7%
Neurosurgery ICU	2	4.7%
Infectious Disease	2	4.7%
Surgery	2	4.7%
Cardiac Care Unit	1	2.3%
Nephrology	1	2.3%
Neurology	1	2.3%
Pulmunology	1	2.3%
Neurosurgery	1	2.3%

ICU:intensive care unit

Table 3. Reasons for use of Caspofungin in patients.

Reason for use	Frequency	Percent
Unknown	8	18.6%
Empiric for febrile neutropenia	7	16.3%
Empiric treatment for ICU patients with Candida Score > 2.5	6	16.3%
Urinary tract infection	6	14%
Intra-abdominal surgery	5	11.6%
Respiratory tract infection	4	9.3%
Oropharynx infections	3	7%
Mixed Infections	3	7%

ICU:intensive care unit

The culture was not obtained in 20 cases (46.5%). In cases with culture the most common sites from which it was obtained were trachea and urine (16.3% each). The other sites included throat, abdominal secretions, blood (9.3%, 7%, 2.3%, and 2.3%, respectively). Culture results are shown in Table 4. Drug interactions were detected in 12 cases, (27.9%) all of which were with dexamethasone. Normal Saline and dextrose water 5% were the main drug diluents with 79.1% and 9.3%, respectively.

Table 4. Culture results in understudy patients.

Microorganism	Frequency	Percent
No culture obtained	20	46.5%
Unspecified Candida	10	23.3%
Candida Albicans	6	14%
Non-Albicans Candida	7	16.2%

The drug administration in 11 cases (25.6%) occurred in less than one hour. The indication of treatment was incorrect in 12 out of 27 cases (28%). Also the drug administration's continuation was correct in 27 cases (62.8%). Among these 27 correct cases, the 23 positive cultures included 7 cases with tracheal candidiasis, 7 cases with urinary candidiasis, 4 samples with oropharyngeal candidiasis, 3 cases with intra-abdominal candidiasis, one with blood candidiasis, and in one case Candida was isolated from different sites. 31 patients (72%) received both 70 mg and 50 mg of Caspofungin on the first day (more than the appropriate dose) and in 5 cases (11.6%) the prescribed dose on the first day was lower than the correct dose.

Based on Sandford Guideline, one case with hepatic failure (Child-Pugh Classes B) received 35 mg of Caspofungin on a daily basis. The mean treatment duration was 10.88 ± 5.35 days ranging from 2 to 24 days. The duration of treatment was correct in 20 cases (46.5%) and incorrect for 23 patients (53.5%).

Discussion

After assessing Caspofungin's medication pattern in a training referral hospital, an inappropriate pattern of the drug's use without rational rate was detected. It was found that the majority of cases were in ICU. In a Chinese study (17) it was reported that Caspofungin is the drug of choice for patients admitted in ICU due to invasive fungal infections. Also, another study (18) revealed that Caspofungin has better efficacy and more safety in comparison to amphotericin for critically ill patients. However, in our study the prescription rate was only assessed for Caspofungin and there was no comparison

with other medications. The drug may be assessed comparatively in other studies (19). Interestingly, Al Balushi et al., (20) assessed the prescribing pattern of antifungal medications among 1353 cases in Oman. However, none of the examined medications were Caspofungin.

The mean prescription days of Caspofungin was 10.9 ± 5.4 ranging from 2 to 24 days, with incorrect duration in more than half of the cases. But the study by Chandwani et al. (21) carried out on 15739 cases under Caspofungin therapy revealed that the commonly used loading dose was 70 mg for Caspofungin in 57.2 percent of cases, and also showed that the mean dosages and duration were consistent with the recommended loading and maintenance dosages for Caspofungin. However, the role of Caspofungin therapy's inappropriate duration in the development of drug resistance as shown by Thompson et al. (22), should be kept in mind. The main limitation was a small sample size as there were no previous studies similar to ours. This study was only a plain report based on the data available in our center, with the aim of encouraging other Iranian centers to develop better programming for anti-fungal use. But it is necessary to perform another DUE after the educational program on introducing and implementing appropriate guidelines as a way to evaluate the impact of these interventions.

In conclusion, in comparison with Sanford and IDSA Guidelines, there are multiple disparities in Caspofungin therapy such as inappropriate duration, continuation, and indications in Firoozgar hospital. Therefore, these should be announced to the physicians for taking further caution in such cases. It would be better to consult with infectious diseases specialists for the administration of anti-fungal drugs. Also, it is advisable to conduct further studies with more focus on the antimicrobial and antifungal resistance pattern.

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