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Abstract

Background: Extended-infusion cefepime (EIC) has been associated with decreased mortality in adults, but to our knowledge, there are no studies in children. **Objective:** The objective of this study was to determine the feasibility of implementing EIC as the standard dosing strategy in a pediatric population. **Methods:** This was a descriptive study of children aged 1 month to 17 years, including patients in the intensive care unit, who received cefepime after admission to a freestanding, tertiary care children's hospital. Patients were excluded if they were admitted to the neonatal intensive care unit or received cefepime in the outpatient, operating, or emergency department areas. Demographic and clinical data for patients who received cefepime from April through August 2013, the period following EIC implementation, were extracted from the medical records. **Results:** A total of 150 patients were included in the study, with a median age (interquartile range [IQR]) of 6 years (2-12.3 years) and median weight (IQR) of 20.7 kg (13.2-42.8 kg); 143 patients received cefepime via extended infusions, and 10 (7.0%) of those were changed to a 30-minute infusion during treatment. The most common reasons for infusion time change were intravenous (IV) incompatibility and IV access concerns, responsible for 50% of changes. Dosing errors and reported incidents during therapy were sparse (n = 12, 8.0%) and were most commonly related to renal dosing errors and/or initial dose error by prescriber. **Conclusions:** Because 93.0% of the patients who initially received EIC remained on EIC, implementation of EIC as the standard dosing strategy was feasible in this pediatric hospital.

Introduction

Infections caused by multidrug-resistant bacteria are increasing in prevalence in adults and children and are associated with poor clinical outcomes.[1-7] Less commonly used antibiotic classes can be utilized in the treatment of multidrug-resistant bacteria, but many alternatives are less than ideal. Carbapenems should be reserved for the treatment of serious Gram-negative infections resistant to other β-lactams because increasing use may expedite the development of resistance.[8] Fluoroquinolones are conveniently and easily administered antibiotics; however, use quickly promotes the development of resistant bacteria.[8] Tigecycline has been suggested as a treatment option, but its place in therapy is uncertain, particularly with limited experience in children and a boxed warning for increase in mortality.[9] Polymyxins, an older drug class associated with nephrotoxicity concerns, are now being used again as a last resort.[8] Polymyxin dosing information in adults and children is limited, further complicating the treatment of serious Gram-negative multidrug-resistant infections.

Though some new antimicrobials are in development, results from studies in pediatric populations will be expected many years after studies in adults. With limited new antimicrobials targeting resistant organisms available for pediatric use, practitioners must focus on optimizing currently available agents to adequately treat children and improve overall outcomes.[10] Broad spectrum β-lactam antibiotics such as piperacillin/tazobactam and cefepime are commonly used for empirical treatment of infections in hospitalized children. Optimization of cefepime dosing regimens based on pharmacokinetic (PK) and pharmacodynamic (PD) parameters is one option in expanding current use of the medication and limiting further development of antimicrobial resistance.

Extrapolation of data regarding cefepime from adults to children is not simple. The elimination half-life of cefepime is shorter in children aged 2 months to 16 years: 1.3 to 1.9 hours, as compared with 2 to 2.3 hours observed in adults.[11] A larger volume of distribution of cefepime—0.37 L/kg as compared with 0.21 L/kg in adults—is also observed in the pediatric population.[11] Bacterial killing by cefepime is dependent on the length of time that free drug concentrations exceed the minimum inhibitory concentration (MIC; fT>MIC) for the bacterial pathogen.[12,13] Given the more rapid elimination of cefepime in children, strategies to optimize fT>MIC in children are critically important.

Courter et al[14] utilized PK parameters obtained from healthy children and Monte Carlo simulations to demonstrate that commonly recommended pediatric cefepime doses do not achieve adequate PD exposures.[14,15] Cefepime intravenous (IV) doses of 50 mg/kg/dose over 30 minutes every 12 and 8 hours achieved probabilities of target attainment of only 15% and 79%, respectively, for *Pseudomonas aeruginosa* isolates, with MICs of 8 mg/L.[14] However, when cefepime was administered over 3 hours, probabilities of target attainment increased to 57% and 100% with every 12- and every 8-hour dosing, for the same *P aeruginosa* isolates.[14] Despite the potential to optimize the PD of cefepime in children as well as data suggesting tolerability,

efficacy, and improved clinical outcomes in adults, extended-infusion cefepime (EIC) has not been studied in hospitalized children.[16,17] One reason may be concern that extended-infusion β-lactam dosing is not feasible in children; however, Nichols et al[4] demonstrated the feasibility of extended-infusion piperacillin/tazobactam (EIPT) in a pediatric population with 92% of patients continuing on an EIPT regimen. The objective of this study was to determine the feasibility of implementing EIC as the standard dosing strategy in a pediatric population.

Methods

This was a prospective, descriptive study of hospitalized patients receiving cefepime following implementation of the extended-infusion dosing strategy as standard of care at a tertiary care children's hospital. Patients aged 1 month through 17 years who received at least 1 dose of cefepime from April through August 2013 were eligible for inclusion. Patients were excluded if they were admitted to the neonatal intensive care unit (ICU) or received cefepime in the outpatient, operating, or emergency department areas.

Following approval by the institution's Pharmacy and Therapeutics Committee in April 2013, the standard cefepime dose was changed from 50 mg/kg/dose IV every 8 hours, infused over 30 minutes, to the same dose and frequency infused over 4 hours. Doses were capped at 1 g for most indications or 2 g for patients who weighed more than 100 kg or were being treated for central nervous system (CNS) infections. During the study period, cefepime was ordered electronically by prescribers using a specific electronic order form with prepopulated infusion times that also provided decision support for indication and usual adult doses. Although the order set defaulted the infusion time to 4 hours, prescribers were able to manually change the infusion duration to 30 minutes if desired.

Following cefepime initiation, researchers prospectively extracted patient demographic, cefepime indication, and dosing information and cefepime-related outcome data from the patients' electronic medical records. Infections were defined as resolved based on treating physician assessment and documentation and if antibiotic therapy was discontinued at discharge from the hospital or at a follow-up visit with a health care provider. If patients did not have positive cultures and cefepime was discontinued after empirical use, this was defined as "no infection." Febrile neutropenic patients were not included in this category. Death was designated as the outcome if the patient died prior to discharge and the death was possibly caused by the indication for cefepime. If cefepime was discontinued because of decline in clinical condition or persistently positive cultures, the outcome was categorized as unsuccessful. Unknown outcome was selected if there was insufficient documentation to determine the final outcome. Concurrent medications and IV access points on the patient were documented at cefepime initiation and at the time of a dosing change, if applicable. Therapy was defined as targeted if a specific infection was treated (ie, cystic fibrosis exacerbation, positive culture) or empirical if cefepime was administered for febrile neutropenia, for an infection of unknown etiology, or for a "rule-out" course.

Data Analysis

The primary outcome of this study was the feasibility of EIC as determined by the percentage of courses completing the 4-hour infusion instead of changing to the 30-minute infusion. Coadministration feasibility, in the circumstances where cefepime and concurrent IV medications were used, was determined if 2 or more doses of cefepime and the other medications were successfully administered together. Secondary outcomes were infection resolution and safety profile as documented in the medical record. Descriptive statistics were used for patient demographics, percentage of cefepime courses administered via extended infusion, and secondary outcomes. Analyses were conducted using Statistical Package for Social Sciences version 19.0 (SPSS, Inc, Chicago, IL). The study was approved by the Indiana University institutional review board.

Results

In all, 150 children with a median (interquartile range [IQR]) age of 6 years (2-12.3 years) and weight 20.7 kg (13.2-42.8 kg) were included in the final analysis. The most common cefepime indications were febrile neutropenia with or without bacteremia, sepsis or rule-out sepsis, urinary tract infection/pyelonephritis, and cystic fibrosis (CF; Table 1). The hematology/oncology, stem cell transplant, and pediatric critical care services were responsible for prescribing 54.6% of cefepime courses. There were 75 positive cultures among 64 patients (42.7%). Positive cultures were most commonly obtained from the blood, lungs, and urine: 30.7%, 18.7%, and 18.7%, respectively. Gram-negative organisms were reported more frequently than Gram-positive organisms in these body sites (39/52). Some patients had concomitant Gram-negative and Gram-positive infections (9/52). The geometric mean MIC of isolated Gram-positive and Gram-negative organisms for cefepime, when MIC data were available, was 1.3. A cefepime-specific MIC was not documented for each Gram-positive isolate in accordance with laboratory practices, so nonsusceptibility was inferred from oxacillin and ceftriaxone MICs in some cases.[18] Of 39 Gram-negative isolates with documented cefepime MIC values, including 17 *Pseudomonas* isolates, MIC values for 24 isolates (61.5%) were 1 mg/L, 8 (20.5%) values were 2 mg/L, 1 value (2.6%) was 4 mg/L, 4 (10.3%) were 8 mg/L, and 2 (5.1%) were 16 mg/L. For some mucoid *P aeruginosa* isolates, the lab performed Kirby Bauer tests for susceptibility, so MIC values were not known. Microbiological culture data are shown in Table 2. The mean (SD) estimated glomerular filtration rate as assessed via the modified equation suggested by Schwartz et al[19] (mL/min/1.73 m^2) at cefepime initiation was 129 (5). Of the patients treated during the study, 32 (21.3%) were hospitalized in an ICU. The median (IQR) length of stay in the ICU was 3 days (2-6.8 days). Patients receiving EIC were treated for a median duration of 6 days (IQR = 3-10 days; range = 1-35 days) and experienced a median hospital stay of 14 days (IQR = 7-31 days; range = 2-160 days). Patients who received the 30-minute infusion were also treated for a median duration of 6 days (IQR = 3-13 days; range = 2-15 days) and were in the hospital for a total of 13 days (IQR = 4-55 days; range = 2-55 days).

EIC was initiated in 95.3% (143/150) of patients, whereas 4.7% (7/150) initially received the 30-minute infusion. Most patients received every-8-hour dosing, but 10 patients received different intervals because of adjustment for impaired renal function. In all, 133 patients (93.0%) remained on EIC throughout the duration of the cefepime course. Also, 11 patients had the infusion time changed from 4 hours to 30 minutes, and 2 patients had the infusion time changed from 30 minutes to 4 hours. In these cases, the median (IQR) day of change was the fourth day (second to tenth), and the infusion time was changed as a result of IV access issues in 50% (n = 6) of cases. Specific reasons for changing from EIC to a 30-minute infusion were incompatibility/not enough access (n = 2, 18.2%), preventive change by prescriber as a result of potential future access concerns (n = 2, 18.2%), prescriber preference (n = 2, 18.2%), patient freedom (n = 1, 9.1%), planning for discharge (n = 1, 9.1%), and nurse concern that precipitates were forming when multiple medications were coadministered (n = 1, 9.1%). The remaining 2 reasons for changing from EIC to a 30-minute infusion were not documented.

At cefepime initiation, 30% of patients had only peripheral access, 52% had only central IV access, and 18% of patients had both central and peripheral access. Patient IV access and concurrent IV medications are displayed in Table 3. Among all patients receiving additional IV medications, the most common concomitant therapies were antimicrobials, analgesics or sedatives, and antiemetics in 53.3%, 30.7%, and 22.7% of patients, respectively. The most commonly administered concurrent antimicrobials during cefepime treatment were vancomycin (n = 57/150, 38%), aminoglycosides (n = 13/150, 8.7%), and metronidazole (n = 9/150, 6%). Concurrent antimicrobials were not necessarily coadministered in all patient cases. Coadministration in which the antimicrobials were infused at the same time as the cefepime occurred with vancomycin (n = 37/57, 64.9%), aminoglycosides (n = 6/13, 46.2%), and metronidazole (n = 8/9, 88.9%). Though there were 136 patients who received at least one additional IV medication while receiving cefepime, there were no documented complications caused by IV access or incompatibility with the concurrent IV medications.

At the completion of cefepime therapy, 36.7% (55/150) of patients were determined to have had no infection. Of those who had documented or suspected infection, the infectious indication was considered to be resolved in 86.3% (82/95) of patients. Of the remaining 13 patients, 6 patients died, 4 had an unknown outcome because of lack of follow-up information from the primary care physician, and 3 patients required an antimicrobial change based on a decline in clinical condition requiring empirical escalation. Of the 6 deaths, only 2 were possibly caused by infection. One complicated patient with cystic fibrosis exacerbation and sepsis ultimately died. At the time of death, the patient had a positive respiratory sputum culture, including 3 different multidrug-resistant *P aeruginosa* isolates (2 resistant to cefepime and all other antibiotics except colistin and tobramycin and 1 isolate with a cefepime MIC of 16 mg/L) and methicillin-resistant *Staphylococcus aureus.* The other patient was undergoing therapy for relapsed acute myeloid leukemia (AML) prior to development of infection for which the patient initially received cefepime. Unfortunately, prior to completion of therapy the patient's clinical condition declined

and palliative care was initiated. The other 4 deceased patients all died because of a preexisting medical condition, including 2 cases of stage IV neuroblastoma, severe anemia attributed to hemophagocytic lymphohistiocytosis, and multivisceral organ transplant rejection. The 3 patients requiring an antimicrobial change based on a decrease in clinical condition were all being empirically treated for febrile neutropenia. One of the 3 patients developed *Clostridium difficile* infection while receiving cefepime. The other 2 patients had negative cultures; one developed typhlitis and liver abscesses of unknown pathology while receiving cefepime, and the other was treated at an outside hospital for typhlitis several days after discharge and cefepime completion.

Cefepime was commonly used for the management of febrile neutropenia. Positive cultures were present in 28.8% (17/59) of febrile neutropenic patients, most commonly in the blood (13/17). The most common microorganisms in febrile neutropenic patients with a positive culture were *P aeruginosa* (4/17) and *Enterobacter cloacae* (3/17). EIC was completed without infusion time change in 96.6% (57/59) of febrile neutropenic patients. Febrile neutropenic patients received cefepime for a median (IQR) of 9 days (5-15 days) and were hospitalized for a median (IQR) of 27 days (10-33 days).

A total of 12 cefepime dosing errors occurred in 12 (8%) patients. All 12 patients received EIC. Table 4 describes the errors and the suspected root causes. No error-related adverse effects were documented.

Discussion

Infections caused by resistant bacteria or bacteria with reduced susceptibility are increasing in prevalence, making it critical to obtain and maintain adequate antibiotic exposures against the pathogenic microorganism.[1⇓-3] PK studies in adults have demonstrated that extended cefepime infusions result in optimized *f*T>MIC for bacteria with elevated MICs, as have mathematical simulations in both children and adults.[17,20⇓-22] Bauer et al[17] report findings suggesting that EIC reduced mortality rates in adult patients with *P aeruginosa* infections. Overall mortality in patients was significantly lower in patients treated with EIC as compared with a 30-minute infusion time (20% vs 3%).[17] The median length of hospital stay was similar for patients receiving EIC, but for patients admitted in the ICU, the median length of stay was 10.5 days shorter for patients receiving EIC.[17] In addition to improved patient outcomes, optimizing PD properties of β-lactams may delay development of future resistance, though this has proved to be difficult to evaluate. To our knowledge, following PubMed and EMBASE literature database searches, this is the first study evaluating EIC in children. In our cohort, EIC was successfully implemented as the standard dosing strategy and was used in 96% of patients. Less than 10% of patients who were initially started on EIC were changed to a 30-minute infusion time, and just over half of those were because of IV access concerns. The comparison of outcomes in these patients with patients receiving a 30-minue infusion of cefepime was beyond the scope of the current study but is a consideration for future research.

These findings are similar to those from a 2012 EIPT study, which reported that EIPT can be successfully adopted as standard care in a pediatric hospital.[4] In all, 92% of patients involved in the study were able to receive EIPT, which is similar to the results for EIC. Of the 8% in the previous study who did not receive EIPT and instead received a 30-minute infusion, the most common reason was incompatibility with coprescribed vancomycin.[4,23] In the present study, changes from EIC to a 30-minute infusion were primarily a result of IV access concerns. Although these concerns were the reason for change in more than half of the patients, this does represent a small number of total patients (n = 6). Though IV access in children, particularly younger infants, may be difficult to obtain and maintain, the IV access concerns in our cohort are interesting, given that the distribution of IV and peripheral access points and receipt of concurrent IV medications in the patients who received 30-minute infusions were similar to those in patients who received 4-hour infusions. A nursing and provider education campaign focusing on IV access maintenance and cefepime compatibility may be a strategy to maintain 100% use of EIC, but we would not recommend adding additional access for the sole purpose of EIC.

We believe that one key to the success in implementing EIC as a standard dosing strategy in pediatric patients was staff education. Traditional infusion times of 30 minutes have been used in pediatric institutions for many years, and implementing change is challenging. At our free-standing hospital within a larger health care system, implementation of standard EIC followed the same steps as our previous transition to EIPT. The institution's Pharmacy and Therapeutics Committee approved the infusion time change as an automatic interchange at both adult and children's hospitals within the system. Pharmacists were provided a pharmacy-specific educational handout and verbal education with a chance to ask questions during daily pharmacy collaboration meetings. Nurse educators dispersed a nursing-specific educational handout along with verbal education to the nursing staff through usual nursing education routes. Chief medical residents distributed main points of EIC education to the remainder of the medical residents. Required electronic order forms were utilized for cefepime ordering by prescribers with a 4-hour infusion time default. The order forms provided decision support regarding doses in child- and adult-sized patients and a place to document a desire and rationale for shorter infusion times. Continued vigilance and education can be utilized to minimize future errors and prevent prescribers from switching infusion times during treatment because of IV access and incompatibility concerns when there are none. In all, 8 errors that occurred were linked to prescribing, which could have been potentially prevented through education about EIC. Prescribers who erroneously altered treatment infusion times can be reeducated to prevent unneeded changes in future patients. The remaining 4 errors that occurred were more likely a result of other root causes and not a change to EIC.

Positive clinical outcomes without major complications were observed in patients receiving EIC, but comparison of outcomes with patients receiving traditional 30-minute infusions were beyond

the scope of this study. Further studies examining the outcomes of 30-minute infusion and EIC in pediatrics should be performed to allow conclusions regarding safety and efficacy of EIC.

Current lack of comparative outcomes data in children may hinder the adoption of EIC in other pediatric institutions, particularly because this dosing strategy requires increased IV access use and increases the potential for IV compatibility issues with other medications. Anecdotally, the increased time that a patient is attached to an IV pole has not been a problem in our institution, and compatibility issues can be addressed with a change in infusion duration. From a cost perspective, because the dose (50 mg/kg) does not change in smaller patients, no difference in cost is expected. In appropriate patients who weigh >20 kg, without CNS infections, a cost benefit can be realized by capping the dose at 1000 mg IV every 8 hours instead of continuing weight-based dosing up to a maximum of 2000 mg.[21] Specific cost comparison was beyond the scope of the current study.

One strategy might be to use EIC only in critically ill patient populations or in patients infected with organisms with demonstrated elevated MICs. However, elevated MICs and resistance to β-lactams such as piperacillin/tazobactam and cefepime are becoming more common in hospitalized patients.[24] Of the 39 Gram-negative isolates with documented cefepime MIC values in our study, 18% (7 isolates) displayed an elevated MIC of 4 μg/mL or greater. In the study by Bauer et al,[17] >30% of the *P aeruginosa* isolates exhibited an MIC to cefepime of ≥8 mg/L.[17] Though specific MIC distributions were not provided, in the study by Courter et al,[14] the MIC_{90} for *P aeruginosa* isolates in 2 pediatric specialty hospitals was 16 mg/L for cefepime and piperacillin/tazobactam. Because cefepime is frequently initiated prior to isolation and susceptibility testing of an organism, when appropriate antibiotic choice is most important, use of an optimized dosing strategy in all patients lessens the chance of "missing" a resistant organism. Additionally, consistent use of EIC is likely to reduce confusion and drug errors as nurses become accustomed to always infusing doses over 4 hours. Additionally, although EIC may not confer a clear outcomes benefit over traditional infusion in all patients, particularly those infected with organisms with lower MICs, it is unlikely to increase the risk of harm.

Conclusion

Implementation of EIC as the standard dosing strategy was feasible at this children's hospital, with 93% of patients (except those admitted to the neonatal ICU or those receiving cefepime in the outpatient, operating, or emergency department areas per exclusion criteria) continuing to receive EIC. In efforts to optimize antimicrobial dosing and use, other children's hospitals are encouraged to utilize these findings within their institutions. Further studies evaluating the clinical outcomes of EIC would aid in the widespread adoption of this dosing practice.

Article Notes

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Table 1. Patient Characteristics (n = 150).

	n (%)
Male	78 (52)
Median age in years (IQR)	6 (2-12.3)
Age category	
30 Days to <1 year	12 (8)
1 Year to 5 years	59 (39.3)
6-11 Years	39 (26)
12-17 Years	40 (26.7)
Indications for therapy	
Febrile neutropenia	46 (30.7)
Sepsis/Rule out sepsis	14 (9.3)
Urinary tract infection/Pyelonephritis	14 (9.3)
Febrile neutropenia and bacteremia	13 (8.7)
Cystic fibrosis	12 (8)
CNS infection/Meningitis	11 (7.3)
Abdominal infection	10 (6.7)
Bacteremia[a]	10 (6.7)
Skin and soft-tissue infection	5 (3.3)
Surgical prophylaxis	5 (3.3)
Other	10 (6.7)

Abbreviations: CNS, central nervous system; IQR, interquartile range.
[a]Bacteremia in patients who were not febrile and neutropenic.

Table 2. Microbiological Cultures (n = 75).

	n (%)
Blood cultures	23 (30.7)
Enterobacter cloacae	3 (13.0)
Coagulase-negative staphylococci	3 (13.0)
Pseudomonas aeruginosa/Fusobacterium nucleatum	2 (8.7)
Viridans streptococci	2 (8.7)
Escherichia coli	1 (4.3)
Serratia species	1 (4.3)
Klebsiella oxytoca	1 (4.3)
Viridans streptococci/*Staphylococcus aureus*	1 (4.3)
K pneumoniae/Viridans streptococci	1 (4.3)
P aeruginosa	1 (4.3)
P putida	1 (4.3)
Enterococcus faecium	1 (4.3)
Enterobacter cloacae/K pneumoniae	1 (4.3)
K pneumoniae	1 (4.3)
Staphylococcus aureus	1 (4.3)
Capnocytophaga sputigena	1 (4.3)
Microbacterium species	1 (4.3)
Respiratory cultures	14 (18.7)
Staphylococcus aureus	5 (35.7)
P aeruginosa	4 (28.6)
P aeruginosa/ Staphylococcus aureus	3 (21.4)
Escherichia coli	1 (7.1)
Enterobacter cloacae/Staphylococcus aureus	1 (7.1)
Urine cultures	14 (18.7)
Escherichia coli	3 (21.4)
P aeruginosa	3 (21.4)
Enterobacter cloacae	3 (21.4)
K oxytoca	1 (7.1)
K pneumoniae	1 (7.1)
Citrobacter freundii/Viridans streptococci	1 (7.1)
Escherichia coli/Citrobacter freundii	1 (7.1)
Corynebacterium species/Viridans streptococci/*Escherichia coli*/Coagulase-negative staphylococci	1 (7.1)
Abscess cultures	8 (10.7)
P aeruginosa	3 (37.5)
Viridans streptococci	2 (25.0)
Coagulase-negative staphylococci	1 (12.5)
Staphylococcus aureus	1 (12.5)
Viridans streptococci/*Eikenella corrodens*	1 (12.5)
Wound cultures	7 (9.3)
Enterobacter cloacae	2 (28.6)
Staphylococcus aureus	2 (28.6)
P aeruginosa/Viridans streptococci	1 (14.3)
Corynebacterium species/Viridans streptococci/*Escherichia coli*/Coagulase-negative staphylococci	1 (14.3)
Bacteriodes thetaiotaomicron/B fragilis/ Clostridium innocuum/Viridans streptococci/*Escherichia coli/P aeruginosa*	1 (14.3)
CSF cultures	4 (5.3)
Staphylococcus aureus	2 (40.0)
Coagulase-negative staphylococci	1 (25.0)
Enterobacter agglomerans	1 (25.0)
Catheter cultures	3 (4.0)
Staphylococcus aureus	2 (66.7)
Enterobacter cloacae	1 (33.3)
Pleural fluid cultures	1 (1.3)
P aeruginosa/Viridans streptococci	1 (100.0)
Peritoneal fluid cultures	1 (1.3)
P aeruginosa	1 (100.0)

Abbreviations: CSF, cerebrospinal fluid.

Table 3. IV Access and Additional IV Medications.

	EIC (n = 143)	30-Minute Infusion (n = 7)	On the Day of Infusion Duration Change if Change Occurred (n = 12)
IV Access at cefepime initiation[a]			
Arterial catheter	7 (4.9)	0	0
Central access 1	101 (70.6)	4 (57.1)	8 (66.7)
CVC	66 (46.2)	2 (28.6)	5 (41.7)
PICC	24 (16.8)	1 (14.3)	1 (8.3)
Port	10 (7.0)	1 (14.3)	2 (16.7)
Pheresis catheter	1 (0.7)	0	0
Central access 2	5 (3.5)	0	0
Dialysis catheter	3 (2.1)	0	0
CVC	1 (0.7)	0	0
Port	1 (0.7)	0	0
Peripheral IV access	66 (46.2)	6 (85.7)	6 (50.0)
Only peripheral access	42 (29.4)	3 (50.0)	4 (33.3)
Concurrent IV medications			
Antimicrobials	76 (53.1)	4 (57.1)	7 (58.3)
Pain and sedation	44 (30.8)	2 (28.6)	3 (25.0)
Antiemetics	32 (22.4)	2 (28.6)	2 (16.7)
Antihistamines	14 (9.8)	2 (28.6)	2 (16.7)
Steroids	12 (8.4)	0	2 (16.7)
Chemotherapy	11 (7.7)	0	2 (16.7)
Diuretics	10 (7.0)	0	1 (8.3)
Gastrointestinal agents/ Duodenal ulcer treatment	5 (3.5)	2 (28.6)	1 (8.3)
Anticonvulsants	6 (4.2)	0	0
Immunosuppressants	6 (4.2)	0	0
Antihypertensives	5 (3.5)	0	2 (16.7)
Colony-stimulating factors	3 (2.1)	0	0
Blood products	2 (1.4)	0	0
Inotropes	2 (1.4)	0	0
Paralytics	0	0	1 (8.3)

Abbreviations: CVC, central venous catheter; EIC, extended-infusion cefepime; IV, intravenous; PICC, peripherally inserted central catheter.
[a]Reported as n (%).

Table 4. Cefepime Dosing Errors.[a]

Error Type	n	Suspected Cause
Dose inappropriate for patient's renal function	3	Prescribing (unfamiliar with renal dose adjustments)
Frequency incorrect	3	1: System; previous adult dosing regimen of q 6 hours was mistakenly carried forward 1: Prescribing; infusion time changed without corresponding increase in normal adult dose 1: Dispensing; frequency increased because of concern about number of medications through central catheter
Prescribed dose exceeded usual adult dose of 1 g/dose	2	Prescribing (unfamiliar with order form)
Prescribed dose too low	2	Prescribing
Patient did not receive entire cefepime dose	1	Intravenous access began to leak during administration
Missed therapy	1	System, prescribing, order verification; when regimen changed, new regimen scheduled to start a day in the future (patient missed 1 day of therapy)

[a]12 Errors occurred in 12 patients.