

Cefepime versus ceftazidime as empirical therapy for fever in neutropenic patients with haematological malignancies

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Abstract An open randomized comparative study was conducted to evaluate the efficacy of Cefepime (2 gm iv. 8 hr.) vs. ceftazidime (2gm iv. every 8 hr.) in empirical therapy of febrile neutropenic patients. A total of 40 eligible febrile episodes were randomized to be treated with study regimen. Twenty febrile episodes were treated with cefepime and 20 were treated with ceftazidime. The two groups were comparable in terms of age, sex, height, underlying neoplasm, number of pretherapy neutrophils, duration of neutropenia. The overall therapeutic success rate of cefepime group (60%) was comparable to that of ceftazidime group (55%). The results of this study suggest that cefepime is an effective and safe agent in empirical therapy of febrile episode in neutropenic patient and its efficacy is comparable with that of ceftazidime.

Introduction

Myelosuppression is one of the commonest complication of cancer and its treatment [1]. Recent studies have cited a figure of 48.3 infection per 100 in neutropenic patients (<1000 granulocytes per microliter) with haematological malignancies and solid tumours [2]. Cefepime is the first in a class of new broad spectrum cephalosporin and has characteristics required for initial empirical therapy of febrile episodes in neutropenic patients. Its spectrum of activities include ceftazidime susceptible gram negative bacilli and many gram bacilli resistant to ceftazidime [3].

During the past decade, there has been a shift in the predominant pathogens in neutropenic cancer patients, from aerobic gram-positive bacteria to gram-positive organisms, including coagulase-negative staphylococci and streptococcus mitis, often are resistant or only partially susceptible to ceftazidime. This problem, together with the increasing resistance to ceftazidime by gram-negative organisms such as *Enterobacter* spp. and *Klebsiella* spp., has created a need for agents with broader antimicrobial activity [3].

The present study is therefore, undertaken to compare the effectiveness of cefepime with that of ceftazidime as monotherapy for empirical treatment of febrile neutropenia.

Material and methods

The study was conducted in Pt. B.D. Sharma PGIMS, Rohtak on patients of hematological malignancy with neutrophil count of less than 1000 cells/mm³. At least 40 cases of febrile neutropenic with single temperature reading >101°F with haematological malignancy were taken. Patients were divided into two groups of 20 each. First

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Table 1 Types of underlying leukemia cases

	Group I Cefepime (n=20)	Group II Ceftazidime (n=20)
AML	12	14
ALL	6	5
CML with blast crisis	2	1

Table 2 Neutrophil count (cell/mm³) at onset of fever

	Group I Cefepime (n=20)	Group II Ceftazidime (n=20)
Mean	500.5	475
Median	545	400
S.D.	249.49	301.51
Range	120–900	100–1000

P=>0.05 (NS)

Table 3 Duration of neutropenia days before antibiotic

	Group I Cefepime (n=20)	Group II Ceftazidime (n=20)
Mean	5.35	5.3
Median	5	5
S.D.	1.38	1.45
Range	3–8	3–10

p >0.05 (NS)

Table 4 Site of infection

Sr. No.	Site of infection	Group I Cefepime (n=20)	Group II Ceftazidime (n=20)
1.	Lung	2	4
2.	Blood (Bacteremia)	2	3
3.	UTI	2	1
4.	GIT	0	11
	Liver abscess Typhilitis	-	
5.	Oral cavity	3	2
6.	CNS (meningitis)	0	1
7.	Skin (Herpes zoster)	0	1
8.	Catheter site erythrema	2	1
9.	Anal	1	1

UTI - Upper respiratory tract.

GIT - Gastrointestinal tract.

Table 5 Time of defervescence days

	Cefepime (n=20)	Ceftazidime (n=20)
Mean	5.5	6.36
Median	5	6
Range	3–12	3–12
SD	2.83	2.38

P=>0.05 (NS)

group was given cefepime 1–2 gm I/V 8 hourly and second group was given ceftazidime 0.5–2 gm every 8 hourly. Patients over 14 years of age who received chemotherapy for haematological malignancy with febrile neutropenia were included in study. Antibiotics was given for 3 days. If patient become afebrile in 3 days, initial treatment was continued for 4 more days. If fever persisted at 4 or 5 days other antibiotics such as vancomycin or amphotericin B was given in standard doses. Vancomycin was given if criteria for use of vancomycin was met. Treatment response was evaluated at day 3 as excellent, good, mild, no response. Final evaluation was determined at day 7 as excellent, good, no response and recurrent. Parameters analysed were pretreatment characteristics (age, underlying leukemia, pretherapy neutropenia, median/mean duration of neutropenia), treatment response at day 3 and final evaluation at day 7 and number of patients needing additional antibiotics like vancomycin and amphotericin B.

Results

Out of the total 40 patients, who had chemotherapy induced febrile neutropenia 26 were of AML, 11 of ALL and 3 of CML in blast crisis. Overall mean age was 33.25±15.95 years in cefepime group and 41.45±18.33 years in ceftazidime group. Mean neutrophil count at onset of fever was 500±249.49 cells/mm³ in cefepime group and 475.30±1.51 cells/mm³ in ceftazidime group with p>0.05. Mean duration of neutropenia in these randomized selected patients was 5.35±1.35 days in cefepime group and 5.3±1.45 days in ceftazidime group. Most common site of infection found was respiratory tract followed by blood and oral cavity. Most common isolated organism was *S. aureus* followed by *Pseudomonas*, *E. coli* and *Enterobacter*. Mean time of defervescence was 5.5±2.83 days in cefepime group and 6.36±2.38 days in ceftazidime group. Overall clinical response was 60% in cefepime group and 55% in ceftazidime group (p>0.05). Excellent response was seen in 40% of patients of cefepime group and 30% of patients of ceftazidime group. Good response was seen in 20% of patients of cefepime group and 25% of patients of ceftazidime group. Total number of deaths were 3, 2 in cefepime group and in ceftazidime group.

Discussion

Cefepime is a new extended cephalosporin in vitro studies of cefepime have shown its activity against gram positive organism including most strains of methicillin susceptible. *S. aureus*, α haemolytic. Staphylococci and some coagulase

Table 6 Clinical response in febrile neutropenic patients

	Cefepime (n=20)	Ceftazidime (n=20)	P value
Clinical success (i.e. patients having excellent / good response)	12/20	11/20	>0.05 (NS)
Percentage	60%	55%	
No. of deaths	2	1	

negative staphylococci strains. Cefepime also has good antipseudomonal activity which is essential for antibiotics used in neutropenic patients. These studies make cefepime a promising candidate for empirical therapy with febrile neutropenic patients.

In this study, we compared the efficacy of cefepime and ceftazidime as empirical therapy in treatment of febrile episodes in neutropenic patients. Two groups were comparable in terms of demography. The severity of neutropenia (pretherapy neutrophil and duration of neutropenia) were comparable in both groups. The overall therapeutic success rate of cefepime group (60%) and ceftazidime group (55%) which did not differ significantly. Severe studies have compared the efficacy of cefepime vs. ceftazidime in management of febrile episodes in neutropenia patients. The results of other previous studies [3–8] were comparable with our study that cefepime appears to be efficacious as ceftazidime in the management of febrile episodes in neutropenic patients.

Conclusion

The study demonstrates that cefepime is as efficacious as ceftazidime in the initial treatment of febrile episode in

neutropenic patients. Since the study was conducted in small number of patients a larger study is needed in large number of patients to unravel the exact response of these drugs in patients of febrile neutropenia.

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