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REVIEW

Cefepime: A Review of Its Use in the Treatment of Serious Bacterial Infections

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Abstract: Serious bacterial infections with their high bioburden are often difficult to treat. Emergence of drug-resistant bacteria has worsened the situation, and management of these cases has become a therapeutic challenge. Prompt institution of appropriate antibiotic is vital in order to decrease complications and fatalities. Cefepime is a new fourth generation parenteral cephalosporin which holds promise for management of these severe infections. It has been shown to be useful in critical pneumonias, soft and bone tissue infections, urinary tract infections and febrile neutropenia. It eradicates organisms which have shown resistance to other β-lactam antibiotics. It is stable to hydrolysis by the common plasmid and chromosomally mediated β-lactamases. The twice daily dosing and improved efficacy even at low dosage makes it a suitable alternative to ceftazidime and carbapenems. It is well tolerated by all age groups and is safe even for newborns. Cefepime monotherapy gives both a good clinical response and an excellent microbiological clearance. In order to preserve its anti-bacterial potency, prudent use of cefepime is warranted. Research into its efficacy and safety with other β-lactamase inhibitors is ongoing and will benefit mankind.

Keywords: cefepime, serious infections, resistant infections, nosocomial

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Introduction

Serious bacterial infections are increasingly encountered in practice. Most of these are resistant to commonly used antibiotics. They cause enormous morbidity, mortality and economic losses.[1–5] Timely institution of an appropriate antibiotic is vital for better clinical outcomes.[6–9]

Since the last two decades, many strains of *pneumococci, staphylococci, pseudomonas, klebsiella* and other *enterobacteria* resistant to the first-line drugs are seen.[10–18] These 'superbugs' are isolated not only from intensive care setups, old age homes and dialysis units but also from the community.[19] Vancomycin-resistant *enterococci* (VRE) and methicillin-resistant *staphylococcus aureus* (MRSA) are increasingly reported worldwide.[11,17,18] The physicians of today are left with few or no treatment options to deal with these fulminant and notorious infections.

The Cephalosporins

Till a few years ago, second and third-generation cephalosporins were the drugs of choice for severe and life-threatening infections. Cephalosporins are synthesized from cephalosporin C, a natural antibiotic obtained from Sardinian sewage molds.[20] They are classified into four groups based on their antimicrobial activity. The first generation cephalosporins act against gram-positive organisms with limited activity against gram-negative pathogens. The second generation cephalosporins have increased activity against gram-negative bacteria while retaining its potency against gram-positive pathogens. Third generation cephalosporins are weak in their action against gram-positive organisms with enhanced gram-negative coverage.[21] Recent surveillance reports have revealed increased incidence of organisms resistant to third-generation cephalosporins.[15]

Fourth generation cephalosporins which includes cefepime are more broad-spectrum with good activity against both gram-positive and gram-negative organisms.[21] The other members of this group are cefozopran, cefpirome, cefquinone.

Cefepime

Introduction

Cefepime (BMY-28142) is a new semi-synthetic broad-spectrum fourth-generation cephalosporin which has assured success in treatment of severe and multi-drug resistant infections. It has both excellent gram-positive and gram-negative coverage and is a good agent against *staphylococcal* and *pseudomonal* infections. It also acts against β-lactamase producing organisms.[22–24]

Physical and chemical characteristics

Cefepime has an extended antibacterial activity with action against gram-positive bacteria as well as against the *Enterobacteriaceae*. Chemically cefepime is 1-[[(6R, 7R)-7-[2-(2-amino-4-thiazolyl)-glyoxylamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-en-3-yl] methyl]-1-methylpyrrolidinium chloride, 72-(Z)—(O-methyloxime), monohydrochloride, monohydrate (Fig. 1).[25]

Cefepime ($C_{19}H_{24}N_6O_5S_2$) is marketed as freeze-dried cefepime hydrochloride for parenteral use.[26] It is a white to pale yellow powder which is highly water-soluble. It is available as injections for intramuscular or intravenous use in sterile vials as dry mixture of cefepime hydrochloride and L-arginine in strengths of 0.5, 1 and 2 g. Its synthesis involves a number of steps, but simpler and more productive methods to obtain the pure cefepime are being researched into.[27–29]

Spectrum of anti-bacterial activity

Cefepime has wide bactericidal activity. It acts against gram-positive organisms such as penicillin-sensitive *Staphylococcus aureus, Streptococcus pyogenes and Streptococcus pneumoniae*. Multi-drug resistant *pneumococci* are still susceptible to cefepime.[25,30–32] Cefepime has shown good activity against gram-negative bacteria including those that are resistant to ceftazidime, cefotaxime, cefoperazone and aminoglycosides.[33] Most of the β-lactamase and ESBL (extended spectrum β-lactamase) strains of gram-negative bacteria are still sensitive to cefepime. *Haemophilus influenzae*, *Escherichia coli, Pseudomonas aeruginosa, Moraxella catarrhalis*, *Morganella morganii, Proteus mirabilis,*

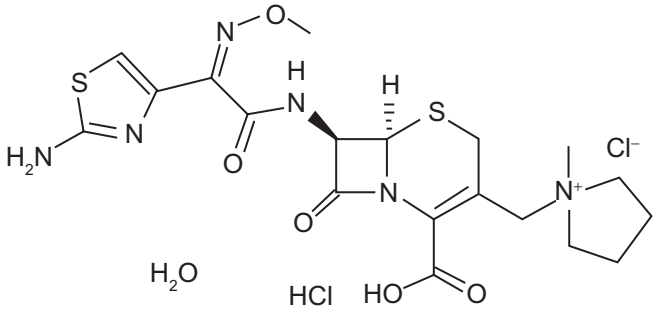

Figure 1. Chemical structure of cefepime.

Acinetobacter, Citrobacter, Enterobacter, Klebsiella, Providencia, Neisseria meningitidis, *Neisseria gonorrhoeae and Serratia* are all susceptible to cefepime.

However, *Enterococcus faecalis, P. cepacia, P. fluorescens*, *Stenotrophomonas (previously Xanthomonas) maltophilia, Listeria monocytogenes, Bacteroides fragilis* are less sensitive to cefepime.[34] Methicillin-resistant *Staphylococcus aureus* and *enterococcus*, and anerobes such as *Clostridium difficile* are resistant to cefepime. Cefepime is also less active against *Citrobacter freundii, Enterobacter cloacae*, and *Serratia marcescens*.[35,36]Amikacin plus cefepime has shown synergistic activity against *P. aeruginosa* strains resistant to cefepime but susceptible to amikacin.[33] The chances of development of new resistance with cefepime are however less because it is a weak inducer of β-lactamases.[37–40]

Mechanism of action

Cefepime inhibits bacterial cell wall synthesis. Compared to other cephalosporins, it penetrates outer membrane of gram-negative bacteria faster and better. Its neutral charge and quaternized N-methylpyrrolidine molecule attached to its methylene group at C-3 helps it to bind to penicillin-binding proteins and enhances its entry into the bacteria. Cefepime also has less attraction for the plasmid and chromosomal β-lactamases. Besides, capacity of cefepime to induce type I β-lactamases is limited. All this contributes to augment the efficacy of cefepime against the bacteria.[41] Cefepime use in the pediatric intensive care units in fact decreases the colonization with resistant bacilli.[39]

Pharmacokinetic profile

Cefepime follows linear kinetics after intramuscular (IM) or intravenous (IV) administration. At the therapeutic dose, serum levels of cefepime attained in adults and children are well above the mean inhibitory concentration most of the time. After IM injection, absorption is rapid. Cefepime is 16%–19% protein-bound. Peak plasma concentrations and minimum plasma concentrations of cefepime following a single IV infusion of 500 mg, 1000 mg, and 2000 mg to healthy subjects are as follows: 31.9, 65.1, and 126 μg/ml and 1.0, 2.7 and 4.2 μg/ml respectively. The half life of cefepime is 1.59 (0.46) hours.[30,42–45]

Cefepime is widely distributed in body fluids and tissues. Volume of distribution at steady state is 18.0 ± 2.0 L [0.32 (0.10) liter/kg]. The bioavailability of cefepime after 2 g dose is 100%. Good concentrations of cefepime are reached in respiratory secretions, bronchial mucosal tissue, appendix tissue, peritoneal fluid, bile, cerebrospinal fluid and blister fluid. Hence cefepime is useful in nosocomial bronchopneumonia, cystic fibrosis, intracranial infections and other severe infections.[42–47] However, penetration into breast milk of lactating women is negligible (0.5 μg/ml) following IV dosing with approximately only 0.02% of a daily dose exposed to an infant[48] (Table 1).

Table 1. Average concentrations of cefepime in specific body fluids (mcg/ml) and in tissues (mcg/g).

Body fluid/tissue	Dose and route	No. of patients	Average time of sample post dose (h)	Average concentration (mcg/ml or mcg/g)
Appendix	2 g IV	31	5.7	5.2
Bile	2 g IV	26	9.4	17.8
Blister fluid	2 g IV	6	1.5	81.4
Bronchial mucosa	2 g IV	20	4.8	24.1
Gallbladder	2 g IV	38	8.9	11.9
Peritoneal fluid	2 g IV	19	4.4	18.3
Prostate	2 g IV	5	1	31.5
Sputum	2 g IV	5	4	7.4
Urine	500 mg IV	8	0–4	292
	1 g IV	12	0–4	926
	2 g IV	12	0–4	3120

Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide). But cefepime is primarily excreted unchanged by renal system with elimination half-life of about 2 hours. This is dose-independent. Less than 1% of the administered dose is recovered from urine as NMP, 6.8% as NMPN-oxide, and 2.5% as an epimer of cefepime. Total body clearance of cefepime is 3.01 (1.46) ml/min per kilogram. Its renal clearance is around 96 to 116 ml/min with 72%–80% of the drug being recovered in urine after the injection. Renal clearance is however low in patients with renal insufficiency and in newborns with immature renal function; hence dose adjustment is mandatory in them (Table 2). The half-life of cefepime in hemodialysed patients is 13.5 ± 2.7 hours, and in patients on continuous peritoneal dialysis, it is 19.0 ± 2.0 hours. The excretion of cefepime is mainly in metabolized form in renal impaired patients. In newborns, dose reduction to 30 mg/kg every 12 hours in newborns is appropriate to achieve optimal peak plasma concentrations.[45,49,50]

Continuous infusion of cefepime has been found to be as effective and safe as the intermittent therapy with a pharmacoeconomic advantage of reduced daily dose.[46,51,52]

Dosing and pharmacoeconomics

Cefepime is available as a sterile, lyophilized powder to be reconstituted. L-arginine is added to it to control its pH at 4.0–6.0. It can be administered as IV short infusion (over 30 minutes) or as continuous infusion (over 24 hours) or by IM route. Sterile water or 1% lignocaine can be used to dilute the injection for IM administration. It is stable in peritoneal dialysis solution with dextrose 1.5% for 14 days in refrigerator, seven days at room temperature, and 48 hours at 37 °C.[53]

Studies have shown that cefepime is efficacious and safe at doses of 50 mg/kg (maximum of 2 g) every 12 hours.[25,31,45] In severe and critical infections such as those caused by *Ps. aeruginosa* or other multi-drug resistant bacteria, cefepime may have to be given in dose of 50 mg/kg every 8 hours.[30,42] Hepatic functions do not affect dosing of cefepime. But kidney function determined by the creatinine clearance dictates the dose of cefepime. Patients with creatinine clearance below 60 ml/minute need dose adjustments. Patients on hemodialysis may need supplemental dosing (Table 2). No dosage adjustment is recommended for elderly patients with kidney functions normal for age.[54]

A study by Giamarellou H revealed that 94% of patients with serious nosocomial infections were clinically cured with 1 g twice daily dose of cefepime.[55] Hence cefepime can cure severe infections even at low dosages. The exact dose required is calculated based on the severity of infections, susceptibilities of the offending organisms and renal function.

Paladino performed a retrospective economic analysis between cefepime and ceftazidime. Cefepime was commonly administered 12 hourly while ceftazidime needed to be given every 8 hours. Over a median duration of 8 days, a median dose of 14 g of cefepime and 24 g of ceftazidime was infused. Clinical success rates and side-effects were similar in both arms. Thus cefepime may be a cost-effective alternative compared to third-generation cephalosporins.[56] It also is a cheaper option to carbapenems.[57,58]

Table 2. Recommended dose of cefepime in renal failure.

Creatinine clearance (ml/min)	Recommended maintenance schedule			
>60	500 mg q12h	1 g q12h	2 g q12h	2 g q8h
30–60	500 mg q24h	1 g q24h	2 g q24h	2 g q12h
11–29	500 mg q24h	500 mg q24h	1 g q24h	2 g q24h
<11	250 mg q24h	250 mg q24h	500 mg q24h	1 g q24h
Hemodialysis	1 g on day 1, 500 mg q24h thereafter			1 g q24h
CAPD	500 mg q48h	1 g q48h	2 g q48h	2 g q48h

Whenever possible, cefepime should be administered at same time each day.
On hemodialysis days, cefepime should be administered after the hemodialysis.

The duration of cefepime administration is usually 48–72 hours after eradication of causative bacteria. This amounts to about 8–10 days *in toto*. Cumulative effect is only seen after a period of 10 days of IV use.[45]

Clinical indications

Cefepime is indicated for use in uncomplicated and complicated urinary tract infections, uncomplicated skin and skin structure infections, abdominal infections, moderate to severe pneumonia, and as empiric therapy for febrile neutropenia. It also cures bacteremic infections. It reverses septic shock and is the drug of choice when infection with *Enterobacter* is suspected or confirmed.[30] Cefepime has demonstrated clinical efficacy in trials involving the lower respiratory tract, urinary tract, skin and soft tissue structures, febrile neutropenia, sepsis and bacteremia, and central nervous system infections. It could be considered as a front-line agent in ventilator-associated pneumonias.[59]

Lower respiratory tract infections

Majority of studies have shown that cefepime reaches optimal concentrations in the respiratory tract of patients with pneumonia. Only 2 studies remarked that cefepime concentrations in sputum were below the MIC required for efficacy.[60,61] In spite of findings of these 2 studies, clinical studies have proven the utility of cefepime in serious pneumonias. McCabe et al compared cefepime with ceftazidime in treatment of moderate-to-severe bacterial pneumonias in two trials. Cefepime was given in dose of 1 g 12 hourly while dosage of ceftazidime was 1 g 8 hourly. In the first open label randomized trial, *H. influenzae*, *S. pneumoniae, P. aeruginosa*, and *M. catarrhalis* were the commonly isolated pathogens. 85% and 72% in the cefepime and ceftazidime groups respectively were clinically cured with similar bacterial eradication rates in both groups. In the second double blind randomized comparison, 15 cefepime and 8 ceftazidime patients were evaluated. There was no statistically significant difference in clinical cure rates and microbiological clearance between both the groups.[62] Holloway and Palmer conducted an open label randomized trial on cases of severe bacterial infections including pneumonias. 53 patients were treated with cefepime 2 g 12 hourly while 49 were managed with ceftazidime 2 g 8 hourly. Clinical response and bacterial eradication were comparable in both arms.[63] Cefepime, in combination with amikacin can also treat cases of mucoviscidosis with bronchopulmonary exacerbation. It leads to marked improvement in lung functional indices and eradication of the causative microbes.[64]

Central nervous system (CNS) infections

Animal studies have shown that around 14.2%–20.2% of cefepime penetrates into the CNS.[65–67] Sáez-Llorens X et al evaluated the role of cefepime for treatment of bacterial meningitis in infants and children. Cefepime at dose of 50 mg/kg 8 hourly was compared with cefotaxime 50 mg/kg 6 hourly. Clinical outcomes were similar in both groups and good concentrations of cefepime were achieved in the CSF in those patients who were on cefepime. There was no *Enterobacter* species isolated in this study.[68] Rousseau JM reported on a 16 year old patient who had *Enterobacter aerogenes* meningitis postoperatively and was managed successfully with parenteral cefepime administered for 3 weeks.[69] Barnes BJ and colleagues have also treated an *Enterobacter cloacae* ventriculitis with cefepime and gentamicin.[70] Thus cefepime appears to be a promising agent for management of CNS infections, especially those due to *Enterobacter species.* Cefepime monotherapy for prophylaxis in neurosurgical patients with external ventricular drain *in situ* is as effective as dual therapy with ampicllin-sulbactam and aztreonam.[71]

Skin, soft tissue and bone infections

Giamarellou H studied 12 patients of skin and soft tissue infections who were administered cefepime in the dose of 1 g 12 hourly. *Enterobacter cloacoe* was the most likely pathogen isolated in them. More than 93% of the cases had good clinical response and demonstrated excellent microbiological clearance.[55] Oster et al in their study on role of cefepime in infections in hospitalized patients had 22 patients of skin and soft tissue infections. They found that 91% and 81% of the cases had clinical and microbiological response respectively with cefepime.[72] Sheng et al also evaluated the efficacy of cefepime in soft tissue infections and found that its use was associated with good clinical outcomes.[6] Jauregui L et al studied patients with osteomyelitis (n = 23), septic arthritis (n = 4) and soft tissue infections (n = 4, 1 with bacteremia)

and concluded that cefepime was safe and effective therapy for osteomyelitis and other severe bacterial infections caused by both Gram-negative and Gram-positive pathogens.[73]

Urinary tract infections

Randomized and double-blind comparative studies of cefepime with ceftazidime for urinary tract infections have revealed that cefepime has clinical and microbiological outcomes similar to ceftazidime.[74] Cefepime also gives good clinical outcome and bacteriologic clearance in serious urinary tract infections including pyelonephritis.[75] A European study on 300 pyelonephritic children also revealed that cefepime had clinical and microbiologic outcomes comparable to ceftazidime.[76] Thus cefepime monotherapy could be a suitable alternative to third-generation cephalosporins for management of complicated or uncomplicated urinary tract infections.

Intra-abdominal infections

Cefepime in combination with metronidazole has been studied in complicated intra-abdominal infections and found to be comparable to imipenem-cilastatin in terms of efficacy and safety.[77] The extended gram-negative coverage of cefepime along with the anerobic coverage provided by metronidazole makes it an attractive combination drug in the therapeutic armamentarium of serious intra-abdominal infections.

Serious bacterial infections

Sheng WH et al assessed role of cefepime in 55 patients (range: 16–94 years) with severe bacterial infections. All had an Acute Physiology and Chronic Health Evaluation II (APACHE II) score of more than 18; 56% of these had nosocomial infections, and 7% had febrile neutropenia. *Ps. aeruginosa* and *Enterobacter cloacae* were most commonly isolated pathogens. Most of these cases had underlying preexisting medical condition and 49% had malignancy. Cure rate was found to be a remarkable 58%. The side effects were seen in only few cases and these too were mild and transient.[6] In another study by Giamarellou H, 239 patients with acute, moderately severe bacterial infections were treated with 1 g of cefepime 12 hourly. Overall, the clinical cure rate for cefepime was 94%. Pathogen eradication was achieved in 93% of infections. In patients with associated bacteraemia, the clinical cure rate was 97% and 94% of the pathogens were eradicated. Cefepime therapy was well-tolerated.[55] Thus cefepime is effective in treatment of serious bacterial infections with or without sepsis syndrome.[78]

Febrile neutropenia

Numerous clinical trials have shown that cefepime, singly or in combination with amikacin, is an effective and safe initial empiric option in febrile neutropenia. It cures more than 95% episodes of fever. There is also shorter defervescence of fever, shorter hospitalization, and lower therapy cost compared to traditionally used antibiotics. Requirement of concomitant systemic antimicrobial therapy (mostly vancomycin) was seen to be less in cefepime patients. There were also fewer new infections in them. Hence cefepime monotherapy seems to score better that the traditional combination treatment of a β-lactam antibiotic with an aminoglycoside for patients of malignancy with febrile neutropenia.[79–84]

Experience in children

Cefepime has been widely used in children >2 months of age. It has also been demonstrated to be effective and safe in newborns.[50,59] Bradley analyzed comparative and noncomparative clinical trials on role of cefepime in serious lower respiratory tract infections in children and concluded that it is effective and safe with an added advantage of broader spectrum of activity against the pathogens.[85] Cefepime also shows good clinical cure rates and microbiological eradication in serious urinary tract infections including pyelonephritis in children.[75] Three hundred and forty-five children 2–14 years old suffering from bacterial meningitis were studied to evaluate the efficacy of cefepime as against cefotaxime or ceftriaxone. It was seen that cefepime was a good alternative as empiric treatment in treatment of meningitis in children.[86] Cefepime can singly replace the other β-lactam antibiotics as initial empiric therapy for febrile neutropenia in children with blood malignancies or solid tumours.[79–84]

Comparative studies

Cefepime fare*s* better than piperacillin against bacteria producing different plasmid-encoded beta-lactamases. Piperacillin was active against these strains only after its

combination with β-lactamase inhibitor, Tazobactam.[32] Stability of cefepime against most β-lactamases makes it a preferred choice when infection with drug resistant bacteria are suspected or confirmed.[87]

Combination therapy vs. monotherapy

Combination of cefepime with an aminoglycoside or fluoroquinolone is useful and safe empiric treatment for serious infections.[88,89] It is supposed to be synergistic; though this synergy is poorly supported. Damas P et al studied cefepime combination therapy vs. monotherapy in ventilator-associated pneumonia and found that addition of an aminoglycoside or fluoroquinolone gave no clinical or bacteriologic benefit. There were no significant differences noted between the two groups as regards the length of stay in the intensive care unit after infection, in ventilator-free days within 28 days after infection or in mortality.[90]

Miscellaneous

Limited studies on use of cefepime in other bacterial infections has proven its utility in cases of *Salmonella paratyphi B* acalculous cholecystitis, in *Enterobacter Cloacae* ventriculitis and for prophylaxis in neurosurgical cerebrospinal fluid pressure monitoring.[70,71, 91]

Adverse Effects and Safety

Cefepime is a well-tolerated cephalosporin. It lacks the nephrotoxicity or ototoxicity of aminoglycosides. However, caution should be exercised when aminoglycosides or loop diuretics such as frusemide are co-administered with cefepime. Renal function monitoring should be carried out in such circumstances.

The side-effects noted with cefepime are mild and related commonly to the skin and gastrointestinal system. Rash, phlebitis, urticaria or pruritus has been noted in a minority of patients. Complaints of loose motions, nausea, vomiting and headache may be present, but its incidence is not more than that reported with other cephalosporins. Neurotoxicity has been reported with cefepime use in post-marketing experiences. Disturbance of consiousness including confusion, hallucinations, stupor and coma, and myoclonus and seizures have been noticed. These cases occurred commonly in patients with renal impairment who received dosages of cefepime higher than that recommended for the creatinine clearance of that patient. But some also were seen with renal impaired patients who were on adjusted dosages. These adverse events were also seen more often in elderly age group patients. Hence caution needs to be exercised in use of cefepime in renal impaired and geriatric patients.

Cefepime may cause some changes in hematological and biochemical parameters of blood. These are usually mild and transient and include fall in hematocrit, total leucocyte count, neutrophils, and platelets. Eosinophils may be increased and there may be some derangements in coagulation profile. Coomb's test may turn positive without hemolysis, and variations may be noticed in liver enzymes, renal profile, calcium, phosphorus and alkaline phosphatase. Hypocalcemia was a common feature in elderly patients on cefepime. Anaphylactic shock is known though rare. Cephalosporin-class adverse reactions such as Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, aplastic anemia, hemolytic anemia, hemorrhage, hepatic dysfunction including cholestasis, and pancytopenia may be seen with cefepime. Hence, cefepime should be avoided in patients with known immediate hypersensitivity reactions to the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics.[30] An IgE type of hypersensitivity to cefepime has been noted.[92]

Cefepime administration leads to a false-positive reaction for glucose in the urine when using Clinitest® tablets but not on enzymatic glucose oxidase reactions (such as Clinistix®).

A suspicion of increased risk of mortality with cefepime was raised in a meta-analysis performed by Yahav D et al in 2007.[93] However, a detailed investigation by the US FDA revealed that cefepime was not linked to these deaths. The US FDA studied a total of 88 trial level and patient level data and concluded that there was no higher rate of mortality in the cefepime-treated patients.[94] Fisher BT et al also studied mortality in pediatric acute myelogenous leukemia patients treated with cefepime, ceftazidime, antipseudomonal penicillin and carbapenems. They found that cefepime was not linked with higher hazard ratio for death.[95] Thus cefepime is a safe and valuable anti-infective therapy for approved indications.

Current Status

Though cefepime has a low propensity for selection of resistant strains and offers a low potential for induction of bacterial resistance, its sensible use is advised. It should be reserved for management of serious systemic infections and for nosocomial infections. It could be a very good selection for initial empiric therapy in febrile neutropenia. Multi-drug resistant infections could be managed successfully with cefepime monotherapy. It is to be preferred in infections where *Enterobacter* is highly suspected and confirmed. It is a life-saving drug for the patients suffering from serious infections treated by oncologists, pediatricians, physicians and surgeons.

Future Developments

Addition of β-lactamase inhibitor such as clavulanate, tazobactum or sulbactum to cefepime tends to widen its anti-bacterial spectra and make it an attractive alternative to carbapenems against ESBL-producers.[96,97] Combination of cefepime with newer metallo-β-lactamase inhibitor could also enhance its anti-bacterial coverage.[98] The disadvantage of insensitivity of anerobes to cefepime could be overcome by addition of linezolid to cefepime-tazobactum combination. This drug is under study and may yield good results.[99]

In spite of all the benefits of cefepime in serious infections, its judicious use is warranted. The declining antibiotic research and development at a time of increasing emergence and spread of resistant pathogens poses a major challenge to our society. If we are to avoid a return to the pre-antibiotic era for many infections, we need to develop sensible strategies to counteract the looming problems. Enforcement of infection control practices may buy time, but ultimately, rational antibiotic usage and heightened research for newer strategies to combat infections are needed.

Conclusion

Cefepime has unique advantages as an anti-infective agent for serious, critical, life-threatening and multi-drug resistant infections. Research into furthering its advantages and emphasis on rational use will assist to preserve its usefulness for years to come.

Disclosure

This manuscript has been read and approved by the author. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The author reports no conflicts of interest.

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