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Clinical Evaluation of Moxalactam

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Moxalactam was administered intravenously or intramuscularly or both in doses of 1 to 12 g/day to 45 patients with clinically significant infections (17 soft tissue or bone, 9 pleuropulmonary, 9 septicemic, 6 urinary tract, and 4 intraabdominal infections). Mean 0.5-h postinfusion levels were 105 μg/ml for a 4.0-g dose, 44.7 μg/ml for a 2.0-g dose, and 18 μg/ml for a 1.0-g dose. We identified 28 isolates of *Enterobacteriaceae*, 10 *Pseudomonas aeruginosa* isolates, 9 *Staphylococcus aureus* isolates, and 15 anaerobic bacterial isolates. A total of 15 patients were clinically cured, 8 patients improved, 13 patients improved initially but suffered subsequent relapses or superinfections, and 10 patients failed therapy. Toxicity was generally minimal (reversible eosinophilia, mild liver function abnormalities, and elevated prothrombin time). The selection or emergence of resistant organisms in 17 patients during treatment (particularly *Pseudomonas*, enterococci, and *Candida*) was a disturbing feature of therapy. Our results were generally favorable, considering the complicated underlying medical problems of this group of patients.

The use of moxalactam (LY-127935) in the treatment of a wide spectrum of bacterial infections has been described previously (8, 11, 12, 19, 21). However, specific data on susceptibility tests, serum levels, and cultures for anaerobes have been lacking from some of these studies.

In this paper we describe the results of a study in which 45 patients were treated with moxalactam for a variety of serious infections. We were particularly interested in the overall effectiveness of this antibiotic, its efficacy against anaerobic infections, and the problem of resistant organisms encountered during therapy.

MATERIALS AND METHODS

A total of 45 infectious episodes were treated in 44 patients (referred to below as 45 patients) hospitalized at the Veterans Administration Wadsworth Medical Center from November 1979 through July 1981. Informed consent was obtained from patients or next of kin before therapy.

The criteria for inclusion in this study included fever and other signs and symptoms of bacterial infection (pneumonia, urinary tract infection, cellulitis, osteomyelitis, intraabdominal infection, septicemia) and either the isolation of a pathogen susceptible to moxalactam (≥20 mm) by standardized disk testing (2) or the high likelihood of obtaining a positive culture with a susceptible pathogen before or during therapy. Patients specifically excluded from the study included (i) patients with organisms resistant to moxalactam (in cases in which mixed infections with both susceptible and resistant organisms occurred, therapy was initiated if the predominant pathogen was susceptible; however, these patients were followed carefully for any sign of deterioration, (ii) moribund patients, (iii) patients with a history of significant allergic reaction to penicillins or cephalosporins (e.g., hives, wheezing, hypotension), and (iv) patients with a neutrophil count of <1,000 cells per mm^3. Patients who had received antibiotics previously were included if the infecting organisms were resistant to the agents used previously and the patient had failed to respond to therapy. Concurrent treatment with antimicrobial agents was not undertaken except for antituberculous chemotherapy or erythromycin therapy for Legionnaires disease (9) when the isolates from the patient (not *Legionella* sp. or mycobacteria) were resistant to these agents and susceptible to moxalactam.

The criteria used for identifying septicemia were positive blood cultures accompanied by fever, chills, or hypotension (blood pressure, ≤90 mm of Hg). The criteria used to diagnose pneumonia included (i) roentgenological evidence of new infiltrate not otherwise explained and (ii) isolation of an organism from transtracheal aspirate, pleural fluid, bronchial brushing, or suitable expectorated sputum (leukocytes present with few or no squamous epithelial cells). The criteria used to identify urinary tract infections included the presence of $>10^5$ cells per ml in clean-catch or catheterized urine specimens, accompanied by signs and symptoms of urinary tract infection (fever, chills, frequency, dysuria). Identification of a cellulitis or soft tissue infection required isolation of an organism from

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wound drainage, accompanied by evidence of soft tissue infection (inflammation, fever, chills, pain).

Patients treated for osteomyelitis had had roentgenograms demonstrating evidence of osteomyelitis taken within 48 h of initiation of therapy. Patients also frequently had positive technetium bone and ^{67}gallium scans. Cultures were obtained whenever possible by bone biopsy (five patients); however, for nine patients sinus tract cultures were relied upon. Patients with intraabdominal infections had cultures taken from intraabdominal abscesses at the time of surgery (or from abdominal-cutaneous sinus tracts) and had active signs and symptoms of infection (fever, chills, abdominal pain).

Patients were classified by clinical and microbiological criteria as cured, improved, improved with relapse or reinfection, or failed. Cured patients had one or more negative follow-up cultures (generally within 1 week of the end of treatment) and a satisfactory clinical response and required no further antimicrobial therapy. Improved patients had a clinical response to therapy but were left with chronic infections which required further long-term antibacterial treatment (e.g., long-term oral treatment for chronic osteomyelitis). Patients were classified as improved with reinfection or relapse if they initially responded to therapy but signs and symptoms of infection with either a different pathogen or the same pathogen recurred after the course of antibiotics. Finally, a treatment course was considered a failure if (i) the patient did not respond to moxalactam, (ii) the patient died after ≥48 h of therapy, (iii) resistant organisms emerged during therapy and required a change in therapy, or (iv) a side effect developed that required interruption of moxalactam therapy. Patients were evaluated for efficacy or toxicity or both if they received more than 48 h of treatment and pretreatment cultures yielded susceptible organisms.

Moxalactam was supplied in 1-g vials. When this antimicrobial agent was administered intravenously (i.v.), the requisite amount of drug (dissolved in 10 ml of sterile water per g) was added to 50 ml of 5% dextrose in water and infused over a period of 30 min. Intramuscular administration was also used in doses of less than 1 g. Doses for patients with normal serum creatinine levels ranged from 1 to 12 g/day; doses for most patients ranged from 1 to 4 g/day. Patients with abnormal renal function received reduced doses based on previous pharmacokinetic data (4).

A complete blood count with differential and determinations of prothrombin time, partial thromboplastin time, blood urea nitrogen, creatinine, serum electrolytes, alkaline phosphatase, serum glutamic pyruvic transaminase, total bilirubin, calcium, phosphate, and urinalysis were obtained within 48 h before therapy, during therapy, and at least once each week after therapy. Fifteen patients also had platelet counts determined.

The concentrations of moxalactam were measured in samples of serum 0.5 h after completion of i.v. infusion or 1 h after intramuscular administration and 0.5 h before the start of the next infusion. These measurements were generally repeated once during the course of therapy. Concentrations were measured by an agar diffusion method, using *Escherichia coli* ATCC 10536 as the control strain (5).

As a screening procedure, susceptibility testing was performed initially by the single disk method (3). All isolates were saved, and minimal inhibitory concentrations (MICs) for the aerobic and facultative organisms were determined by an agar dilution method (6), using *E. coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923 as control strains. The mean magnesium content of freeze-thawed samples of agar was 1.79 mg/100 ml (range, 2.43 to 1.51 mg/100 ml), and the mean calcium content was 2.82 mg/100 ml (range, 3.46 to 2.37 mg/100 ml). Agar dilution susceptibility testing of anaerobes was performed by previously described methods (18). Organisms were considered resistant to gentamicin and tobramycin if the MIC was ≥16 μg/ml, resistant to amikacin if the MIC was ≥32 μg/ml, resistant to cephalothin if the MIC was ≥32 μg/ml, and resistant to moxalactam if the MIC was ≥64 μg/ml (1, 5).

RESULTS

Clinical response. The patients in this study included 43 men and 2 women whose ages ranged from 25 to 84 years (mean, 58.4 years). At the start of therapy all patients were considered to be in either serious or fair condition; thus, none was in critical or good condition. Almost all of the patients had ultimately fatal diseases. A total of 19 had failed to respond to previous antimicrobial agent therapy (usually cefazolin or gentamicin). Table 1 shows the types of infections treated and a summary of the responses to therapy. The duration of therapy was 4 to 65 days (mean, 24.4 days).

Nine patients were treated for septicemia. Only the bacteremia was evaluated in this study, although most patients also had infections at primary sites (Table 2). Of the nine cases described below, two were considered failures. One patient had aortic valve endocarditis secondary to infection with a highly susceptible *Haemophilus parainfluenzae* strain (MIC, <0.12 μg/ml; minimal bactericidal concentrations, 0.12 and 8 μg/ml for the large and small colony types, respectively) and initially responded to high-dose moxalactam therapy (12 g/day); the serum levels were 132.5 μg/ml 0.5 h after infusion and 28.2 μg/ml before the next infusion. The addition of an aminoglycoside to the regimen was required because of recurrent fever, and moxalactam therapy was considered a failure. Another patient had *Pseudomonas aeruginosa* bacteremia and pneumonia, and a strain susceptible to moxalactam (MIC, 32 μg/ml) was isolated. This patient initially responded to moxalactam treatment, but therapy was changed to tobramycin and ticarcillin after development of recurrent fever and clinical deterioration. This case was considered a moxalactam failure although blood cultures while the patient was on moxalactam were negative. Two patients had septicemia associated with infected intravenous catheters. Another patient had polymicrobial bacteremia (*Enterobacter cloacae, Klebsiella pneumoniae*)

TABLE 1. Summary of results with moxalactam

Type of infection	No. of patients	Total no. favorable (cured + improved)	No. cured	No. improved but with clinical superinfection or relapse	No. improved	No. of failures
Septicemia	9	6	6	1	0	2
Pleuropulmonary[a]	9 (2)[b]	7 (1)	3	4	1 (1)	1 (1)
Febrile urinary tract	6	4	2	2	2	0
Soft tissue, bone, and joint	17 (11)	7	2 (2)	4 (3)	5 (2)	6 (4)
Intraabdominal[c]	4 (2)	2 (2)	2 (2)	2	0	2

[a] Three patients with aspiration pneumonia, four with empyema, one with a lung abscess, and one with *Streptococcus pneumoniae* pneumonia.

[b] The numbers in parentheses indicate the numbers of anaerobic infections.

[c] One patient with a sub-diaphragmatic abscess, one with a pelvic abscess, one with a peri-appendiceal abscess, and one with a biliary fistula.

associated with tuberculous enteritis. Two patients had urosepsis.

In addition to the two patients with urosepsis, six other patients were treated for urinary tract infections. All but one had complicated urinary tract infections (obstruction, prostatitis, indwelling Foley catheter). One patient had prostatitis with a resistant *P. aeruginosa* strain (MIC, >128 μg/ml); however, this patient responded with prompt defervescence. Urinary levels of moxalactam were not determined. Two of these six patients developed problems with emergence of resistant organisms while on moxalactam therapy. One patient developed *Candida albicans* cystitis and required treatment with amphotericin B (bladder irrigations). Another patient developed an enterococcal urinary tract infection and required ampicillin therapy.

Nine patients had pleuropulmonary infections (Table 1). Two of these patients had complicated courses after surgery for esophageal carcinoma (esophagogastrectomy), in which they developed esophageal leaks, mediastinitis, and empyema. One patient had a pretreatment isolate of *P. aeruginosa* that was initially susceptible to moxalactam (disk, >20 mm); however, cultures taken on the day that treatment was initiated subsequently showed resistance (MIC, 128 μg/ml), and therapy was changed to gentamicin with ticarcillin when his clinical condition deteriorated. One patient with necrotizing pneumonia secondary to a *K. pneumoniae* infection failed to

TABLE 2. Results of moxalactam therapy in septicemic patients

Patient	Age (yr)	Underlying disease	Source of septicemia	Organism(s)	Length of therapy (days)	Clinical response
1	48	Alcohol abuse	Osteomyelitis	*Streptococcus sanguis*	39	Improved
2	51	Pinealoma; congestive heart failure, Legionnaires disease	Pneumonia	*P. aeruginosa* (MIC 32 μg/ml)	4	Failure
3	45	Chronic pancreatitis	Pancreatic pseudocyst	*K. pneumoniae*	17	Cured
4	43	Disseminated tuberculosis	Intravenous cannula	*Serratia marcescens*	10	Cured
5	39	Multiple sclerosis	Urinary bladder	*E. coli* (resistant *E. coli* [MIC, > 128 μg/ml]), enterococci (MIC, > 128 μg/ml) in urine after treatment	14	Improved with reinfection
6	69	Alcohol abuse	Endocarditis	*Haemophilus influenzae*	57	Failure[a]
7	61	Congestive heart failure; status postmitral valve replacement	Intravenous cannula	*S. aureus*	30	Cured
8	58	Benign prostatic hypertrophy with urinary tract obstruction	Urinary bladder	*Proteus mirabilis, E. coli, Citrobacter freundii*	20	Cured
9	66	Disseminated pulmonary tuberculosis with gastrointestinal involvement	Gastrointestinal tract	*E. cloacae, Klebsiella oxytoca*	10	Cured

[a] See text.

Table 3. Susceptibility test results with aerobic and facultative isolates

Organism	No. of isolates	% Susceptible at breakpoints[a]				
		Moxalactam	Amikacin	Tobramycin	Gentamicin	Cephalothin
P. aeruginosa	18	72	94	87	70	0
E. coli	14	93	100	100	100	75
Proteus sp.	11	72	100	100	100	73
Enterobacter sp.	8	85	100	100	100	0
Klebsiella sp.	5	100	100	100	80	60
Serratia marcescens	4	75	100	100	100	0
Citrobacter freundii	4	75	75	75	100	20
Morganella morganii	2	0	100	100	100	0
Other gram-negative rods[b]	5	100	50	50	50	60
S. aureus	8	100	100	100	100	100
Staphylococcus epidermidis	5	60	60	80	60	75
Enterococci	5	0	0	60	80	40
Other streptococcal species	6	100	40	80	50	100

[a] See text for breakpoints.
[b] Includes *Moraxella* spp., *H. parainfluenzae*, *Pseudomonas maltophilia*, and *Providencia stuartii*.

respond to ampicillin but responded to moxalactam.

Four patients treated with moxalactam had intraabdominal infections. Two of these required surgery for abscess drainage. One of the four had a right lower quadrant peri-appendiceal abscess that yielded numerous anaerobes (including *Bacteroides fragilis*) and required a total of 22 days of treatment. A second patient had a left sub-diaphragmatic abscess secondary to a *Fusobacterium necrophorum* infection and also required surgery. A third patient had a perforated bladder and a pelvic abscess due to *P. aeruginosa* and *E. cloacae*. This patient initially responded to a course of moxalactam but later aspirated and died from bilateral aspiration pneumonia. The fourth patient had a choledochocutaneous fistula after previous biliary tract surgery. This patient failed to respond to an aminoglycoside; however, he became afebrile, and the fistula closed on moxalactam.

A total of 17 patients were treated for osteomyelitis and soft tissue infections. Of the 14 patients with osteomyelitis, 8 had underlying peripheral vascular disease or diabetes mellitus. These patients had particularly poor long-term prognoses, although they initially responded to therapy and were considered improved or cured with relapse. Seven of the eight eventually required amputation. The other six patients with osteomyelitis improved during therapy, and none required amputation; however, no patient with osteomyelitis was cured. Three patients had soft tissue infections (infected human bite wound, infected decubitus ulcer, cellulitis), and these patients all responded to moxalactam therapy.

Anaerobic infections. Anaerobes were isolated from 15 patients; 14 of these patients had mixed aerobic-anaerobic infections. The one patient with a pure anaerobic infection had an intraabdominal abscess with a susceptible *F. necrophorum* strain. This patient responded to surgical drainage and treatment with antibiotics. The responses to treatment were heavily influenced by the large number of patients with bone and soft tissue infections (11 patients), many of whom had underlying diabetes mellitus or peripheral vascular disease (6 patients). Four of these six patients initially had vascular gangrene, and five eventually failed therapy. In general, patients with resistant aerobes or anaerobes were more likely to fail therapy; however, there were patients with completely susceptible organisms who failed therapy.

Susceptibility testing. The results of susceptibility testing of aerobic isolates are shown in Table 3, and the anaerobic susceptibility data are shown in Table 4.

Emergence of resistant organisms. During therapy 31 resistant organisms emerged in 17 patients; 12 patients developed either a relapse of their previous infection with a resistant organism of the same species or a superinfection with a new resistant organism. One patient, who was treated for an empyema which contained (among other organisms) a susceptible *Moraxella* sp. strain, developed septicemia several days after therapy was stopped and died with a highly resistant *Moraxella* sp. isolate (MIC, >128 μg/ml). One patient developed *Candida* fungemia from a urinary tract source, and two patients developed candidal cystitis which required amphotericin B therapy (bladder irrigation). The most common resistant organisms to emerge during therapy were *P. aeruginosa* (14 isolates) and enterococci (9 isolates). Three patients developed resistant *B. fragilis* group strains, and these patients either relapsed or failed therapy.

TABLE 4. Susceptibility of anaerobes to moxalactam

Organism	No. of initial isolates	% Susceptible
B. fragilis subsp. *fragilis*	4 (3)[a]	100 (66)
B. fragilis subsp. *ovatus*	1 (2)	0
B. fragilis subsp. *distasonis*	1 (1)	0 (0)
B. fragilis subsp. *thetaiotaomicron*	1 (1)	100 (0)
Bacteroides melaninogenicus group	6	100
Bacteroides capillosus	1	100
Bacteroides ureolyticus	1	100
Other *Bacteroides* sp.	8	100
Fusobacterium sp.	3	100
Peptococcus sp.	3 (1)	100 (100)
Peptostreptococcus sp.	5	100
Actinomyces sp.	2 (1)	100 (100)
Eubacterium sp.	1	100
Clostridium innocuum	1	100

[a] The numbers in parentheses indicate the numbers of follow-up isolates and the corresponding percentages susceptible to moxalactam.

Serum levels. The concentrations of moxalactam in sera were measured in 38 patients. The mean concentrations 0.5-h postinfusion were as follows: 105 μg/ml for 4.0-g i.v. doses given every 8 h, 42.3 μg/ml for 2.0-g i.v. doses given every 8 h, and 47.1 μg/ml for 2.0-g i.v. doses given every 12 h. The highest levels (mean 0.5-h postinfusion level, 132.5 μg/ml; trough level, 28.2 μg/ml) were obtained in one patient treated with 4 g of moxalactam every 8 h for *H. parainfluenzae* endocarditis.

Toxicity and adverse reactions. In general, patients experienced little toxicity and few side effects. The most common adverse reaction was the development of eosinophilia (10 of 45 patients). One patient developed 28% eosinophilia (leukocyte count, 9,800 cells per mm^3) during therapy, but most values ranged from 6 to 15%. The eosinophilia resolved in all patients when therapy was discontinued. Five patients developed abnormalities in liver function tests (most commonly a mild increase in alkaline phosphatase levels), but there were no associated symptoms. One patient developed moderate thrombocytosis during therapy (552,000 cells per mm^3). This most alarming side effect occurred in one patient who exhibited a prolonged prothrombin time after 4 days of therapy with 2 g of moxalactam given i.v. every 12 h. This patient had massive bleeding from a small lesser curvature gastric ulcer and ultimately required a subtotal gastrectomy despite correction of clotting times with fresh frozen plasma and intramuscular vitamin K_1. Prolongation of the prothrombin time caused no problems in another patient. Three patients developed mild leukopenia (mean leukocyte count, 4,100 cells per mm^3; 58% granulocytes), but this disappeared when the moxalactam treatment was discontinued or while therapy continued. In no patient was it considered necessary to discontinue the drug because of a laboratory abnormality or side effect.

DISCUSSION

It has been hoped that as relatively nontoxic agents with a broad spectrum of activity, the newest cephalosporins (e.g., moxalactam) would prove to be effective against a wide range of bacterial infections, including those due to *P. aeruginosa*. In this study moxalactam was usually effective in treating bacteremic patients when the pathogen was initially susceptible to moxalactam. One of our failures had an organism with borderline susceptibility (MIC, 32 μg/ml; disk, 20 mm) and deteriorated after initially responding to moxalactam treatment. Our experience with pleuropulmonary infections was less favorable than that of other investigators (11); this was perhaps due to patients with "complicated" pleuropulmonary infections who required long courses of therapy and had a propensity to develop resistant organisms.

Previous studies have shown that moxalactam is eliminated primarily via the kidney (17). High urinary levels are attainable, often far above the MICs for susceptible organisms. Moxalactam appeared to be an effective agent for the treatment of urinary tract infections in most of our patients. Both patients considered to have clinical reinfections had their initial pathogens eradicated but developed superinfections with organisms resistant to moxalactam (i.e., *Candida* and enterococci).

Our experience with patients with osteomyelitis and soft tissue infections was not as favorable as our experience with the other patients. One factor which influenced our results was the large number of patients (eight) with osteomyelitis related to underlying diabetes mellitus or peripheral vascular disease. Seven of these patients eventually required amputation, although some initially improved during therapy. Similar results with other agents have been well documented previously (20).

The results with mixed anaerobic infections also may have been influenced by the number of patients with osteomyelitis and underlying diabetes or peripheral vascular disease. Of the six patients in this group who failed therapy, two began therapy with resistant anaerobes. The ultimate success of therapy appeared to be related more closely to the presence of peripheral vascular disease. The two patients with intraabdominal abscesses with anaerobes did well with appropriate drainage and moxalactam therapy.

One problem noted during this study was the occasional misleading results of disk susceptibility tests. One patient had an organism susceptible as determined by disk testing several days before the initiation of moxalactam therapy; however, highly resistant organisms were found in cultures taken on the first day of therapy. It is conceivable that this variation in susceptibility represents random sampling of a mixed population of organisms. Likewise, organisms may appear to be susceptible by disk testing but be resistant when MICs are determined. This may not be a common problem, but it is noteworthy. Any patient who fails to respond to moxalactam treatment may have a resistant organism, and it is wise to check the MICs of isolates from seriously ill patients and patients who fail to respond to the antibiotic.

Our results of susceptibility testing emphasize that there is a wide range of in vitro effectiveness of moxalactam against aerobic and facultative bacteria, but they also show that there are potential gaps in activity. Although most gram-negative bacilli appeared to be quite susceptible to moxalactam, there was a significant degree of resistance (28%) among *P. aeruginosa* strains. If an investigator suspects a serious infection due to *P. aeruginosa*, it would be wise to use a consistently more active agent (i.e., an aminoglycoside) until the results of susceptibility tests are known. This concern has also been raised by other investigators (21) and is supported by the results of some in vitro susceptibility studies (2, 13).

The anaerobic susceptibility data presented above mirror the in vitro testing done in our laboratory, in which a large number of anaerobes were tested against moxalactam (16). A significant percentage (29%) of the *B. fragilis* group species tested were resistant to moxalactam, and caution should be exercised when moxalactam is used against infections potentially due to these organisms. Since we encountered only one *Clostridium* sp. strain, we cannot comment on the role of moxalactam in the therapy of clostridial infections, but many clostridia are resistant in vitro (16).

A disturbing feature of moxalactam use is the emergence of resistant organisms during therapy. This may arise from mixed flora or from a culture with a single species isolated. In this study a total of 17 patients developed resistant organisms while on therapy. In 12 patients these isolates were clinically significant since they resulted in relapse with a more resistant organism or reinfection with a resistant bacterium. The organisms most likely to emerge include enterococci, *P. aeruginosa*, and *Candida* sp. Our experience with enterococci is similar to that recorded in a recent report, in which enterococcal superinfection and colonization occurred in a number of patients during or after moxalactam therapy (22). The emergence of resistant *P. aeruginosa* was also noted in another study (21).

In general, the toxicity of moxalactam appears to be minimal. The high frequency of eosinophilia observed appeared to be clinically benign and disappeared when therapy was discontinued (as did the abnormalities in liver function). In one of the two patients with elevated prothrombin time, the coagulation abnormality appeared to play a major role in exacerbating a gastrointestinal bleeding episode. This effect may have been due to the purported interference of moxalactam with hepatic prothrombin production or to suppression of vitamin K-producing bacteria in the gut. This may be a particular problem for patients with already depleted vitamin K stores (elderly, malnourished, debilitated), patients with chronic liver disease or biliary tract obstruction or both, patients with preexisting coagulation abnormalities, or patients with abnormal renal function on high-dose therapy. The manufacturer has now recommended prophylactic administration of vitamin K for the above groups and close monitoring of clotting function (Robert Kammer, Eli Lilly & Co., personal communication).

Our experience with moxalactam was favorable considering the underlying conditions of our patients, and we believe that the broad spectrum and minimal toxicity of this drug make it a significant addition to the therapeutic armamentarium. The ability to penetrate cerebrospinal fluid also makes it a potentially useful agent in treating gram-negative bacillary meningitis (7, 10, 14). This drug does not appear to have significant renal toxicity and can be given in fairly high doses with few major side effects. A potential concern to clinicians treating septic patients is the less-than-optimal activity of moxalactam against infections with *P. aeruginosa*. However, it may have a significant role even in these cases if the organism is known to be susceptible and the patient is monitored closely during therapy for development of potentially resistant isolates (15). Finally, although many commonly isolated anaerobes are susceptible to moxalactam, this drug should be used with caution against potentially life-threatening anaerobic infections since a significant percentage of *B. fragilis* group species and other anaerobes are resistant.

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