Clinical Trial of Cefonicid for Treatment of Skin Infections

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Twenty patients with skin and soft-tissue infections were treated with parenteral cefonicid. Cultures obtained in cellulitis cases from an aspirate of a leading edge of inflammation were positive in 42% of these patients. Pathogens isolated were Staphylococcus aureus (six strains), Proteus mirabilis (one strain), and Streptococcus agalactiae. Adverse effects were pain on intramuscular injection (two patients), rash (one patient), and positive Coombs test (one patient). All side effects were mild and none required discontinuing antibiotic therapy. A single treatment failure occurred in a patient with an undrained perirectal abscess. Cefonicid may be a useful drug in the treatment of skin and soft-tissue infections. The long half-life of cefonicid (4.8 h) is a valuable advantage and may facilitate patient compliance and convenience.

Cefonicid is a new parenteral cephalosporin antibiotic. Similar to other second-generation cephalosporins, cefonicid has excellent in vitro activity against gram-positive bacteria and many aerobic gram-negative bacteria. Previous clinical studies are few, but good responses have been seen with gonococcal urethritis and community-acquired pneumonia (4, 14). Cefonicid has very high serum levels after infusion and a prolonged half-life (4.8 h) allowing for once-daily dosing. These characteristics suggest a role for cefonicid in the treatment of soft-tissue infections.

Patients with skin and soft-tissue infections admitted to Wilford Hall Medical Center, San Antonio, Tex., from September 1981 through March 1982 were treated with 1 g of cefonicid intravenously or intramuscularly every 24 h as a single injection or infusion. A minimum of 5 days of therapy was required for the patient to be considered evaluable. Informed consent was obtained. Eligible patients were those over 18 with no known renal or hepatic disease. Females were included only if pregnancy was not present by clinical and laboratory parameters. Patients were not enrolled if they had a known allergy to penicillins or cephalosporins, antibiotic therapy within 72 h, or concurrent rapidly fatal underlying disease.

Cellulitis was diagnosed clinically by the presence of swelling, heat, and erythema of the involved skin. Pyoderma was present when localized purulent material was surrounded by swelling, heat, and erythema. Chronic extremity ulcers were considered to be infected only when surrounded by a zone of inflammation and accompanied by an oral temperature of >38°C. Cultures were obtained by needle aspiration of purulent material when present in a previously unmanipulated site. When cellulitis was diagnosed, an aspirate of the leading edge of erythema was performed with a ≥18-gauge needle. Specimens were immediately plated on triplates of chocolate, MacConkey, and 5% sheep blood agar. Chopped-meat broth was inoculated with purulent material, and all specimens were incubated at 37°C. Culture and identification of all pathogens was accomplished by standard laboratory methods. Staphylococcus epidermidis was considered a contaminant when present and was discarded. Blood cultures were collected only when directed by the primary physician. Cefonicid susceptibility was determined by the method of Bauer et al. (2) with 30-μg disks. Susceptible, resistant, and intermediate susceptible isolates were defined as those with a zone size of ≥18, ≤14, and 15 to 17 mm, respectively.

Laboratory evaluation on admission included urinalysis, direct and indirect Coombs test, alkaline phosphatase, blood urea nitrogen, creatinine, creatinine phosphokinase, serum glutamic oxalacetic transaminase, bilirubin, and complete blood count. Laboratory evaluation was repeated every 3 days during therapy and after the completion of treatment. Patients were followed for 7 days after completion of therapy.

Twenty patients received the minimum 5 days of therapy (range, 5 to 7 days) and were judged evaluable. The mean age was 25 years, and 14 of 20 (70%) patients were male. Eighteen patients received intravenous therapy, and two received intramuscular therapy with cefonicid. Patients presented most frequently with cellulitis (16 cases). Other presentations were extremity ulcers with surrounding infection (two cases) and...
pyoderma (two cases). Pathogens were recovered in 40% of the patients and were identified as *Staphylococcus aureus* (six cases), *Proteus mirabilis* (one case), and *Streptococcus agalactiae* group B (one case). Needle aspiration of a leading edge of inflammation yielded positive cultures in 5 of 12 (42%) patients in which it was attempted. All isolates were susceptible to cefonicid by disk diffusion. Adverse effects with cefonicid therapy were pain on intramuscular injection (two cases), rash (one case), and positive Coombs test with no detected hemolysis (one case). Mild transaminase elevation was detected on the hospital day 4 in two patients. All transaminase elevations were less than twice the normal level. In no instance did side effects require discontinuing the study drug. The single treatment failure occurred in a patient with cellulitis of the left buttock due to a susceptible strain of *Streptococcus agalactiae* group B. On treatment day 5, low-grade fever continued and a previously undetected perirectal abscess was discovered and drained. This patient promptly defervesced and recovered uneventfully on alternate antibiotic therapy.

Cefonicid is a new second-generation cephalosporin with a spectrum of activity similar to those of other members of its class (3, 6, 12). The prolonged half-life (4.8 h) (1, 10, 11) offers a theoretical therapeutic advantage for infections that are serious or refractory enough to require parenteral therapy. In this study, we tested this theoretical advantage in patients with skin and soft-tissue infections, primarily those with cellulitis. The results of this study demonstrated therapeutic effectiveness of cefonicid in patients with skin and soft-tissue infections. The single failure was apparently due to an unrecognized and undrained abscess.

Our results are similar to those of Marzouk et al., who recently reported therapeutic equivalence of cefonicid and cefazolin in 46 patients with skin infections (J. Marzouk, L. Dall, G. Slutkin, and J. Mills, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 22nd, Miami Beach, Fla., abstr. no. 793, 1982). Lea and colleagues have reported disappointing results in 35 patients with cellulitis; their study suggests that cefonicid is inferior to cefazolin, particularly when *Staphylococcus aureus* is the pathogen (A. S. Lea, O. S. Gould, K. D. Merrill, and L. O. Gentry, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 22nd, Miami Beach, Fla., abstr. no. 794, 1982). Cefonicid is shown here to be relatively nontoxic, with minor side effects. Pain on intramuscular injection is a common occurrence with some cephalosporins (8) and, with cefonicid, may have been related to the large volume (5 ml) required to administer the single daily dose. This side effect may limit the intramuscular route of administration. Positive Coombs tests have been detected in 10 to 15% of patients treated with cephalosporins (9), and its detection here in a single case is not surprising. Mild and transient elevation of serum transaminase has been described frequently with cephalosporin administration in the past (5, 13). Its occurrence in 10% of patients confirms prior observations that it is infrequent.

The effectiveness of cefonicid has been documented in several infections to be equivalent to that of commonly used parenteral antibiotics. Wallace and co-workers have documented the efficacy of cefonicid in community-acquired pneumonia (14). All patients responded, and no serious adverse effects were reported. Prolonged therapeutic serum levels were documented, thus allowing once-daily dosing. In a study in which single doses of penicillin and cefonicid were compared for gonococcal urethritis, Duncan and McBride (4) demonstrated a 94% cure rate for cefonicid and an 88% cure rate for penicillin. Effectiveness in single-dose surgical prophyllaxis has been documented in the mouse model (7) and is the subject of continuing investigation in humans (T. C. Fabian, E. C. Magiante, and S. J. Boldreghini, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 22nd, Miami Beach, Fla., abstr. no. 761, 1982). The prolonged half-life and favorable spectrum of activity have identified cefonicid as a promising prophyllactic agent.

Cefonicid appears to offer major advantages over other second-generation cephalosporins. The convenience of once-daily dosing has the potential for substantial cost savings, with less nursing time required for drug administration and decreased use of certain nonrenewable resources, such as syringes and intravenous fluid and tubing. Patients with certain chronic infections requiring parenteral antibiotics may be able to leave the hospital environment sooner and receive treatment in an outpatient setting, with once-daily injections in a physician's office. This will reduce the opportunity for colonization with resistant hospital pathogens and return patients to employment sooner. Additional studies should be conducted to document the feasibility and potential economy of cefonicid use in the outpatient setting.

**LITERATURE CITED**


