Cefprozil versus Cefaclor in the Treatment of Bronchitis in the Elderly

Lawrence L. Pelletier Jr

Medical Service, Wichita Veterans Administration Medical Center and the Department of Internal Medicine, University of Kansas, School of Medicine, Wichita, Kansas, and the Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, Connecticut, USA

Summary

In a prospective, randomised, nonblinded, multi-investigator trial, cefprozil 500mg twice daily was compared with cefaclor 500mg 3 times daily, both administered orally for 10 days for episodes of bronchitis. A total of 247 patients aged 65 years or older with mild to moderate acute bronchitis or exacerbations of chronic bronchitis were treated in 30 in- and outpatient clinical sites in Europe and North America. Of these, 104 patients did not have a defined bacterial pathogen in pretreatment sputum cultures. Among the 143 other patients, *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella (Branhamella) catarrhalis* were the most frequently isolated bacteria. There was a satisfactory clinical response to treatment in 119 of 156 cefprozil-treated patients (84%) and in 63 of 91 (82%) of those treated with cefaclor. Eradication of the presumed bacterial pathogen occurred in 74 of 89 (83%) cefprozil-treated patients and 35 of 42 (83%) cefaclor-treated patients. Both cefprozil and cefaclor were well tolerated, with possible drug-related adverse reactions in only 16 of 156 (10%) cefprozil-treated patients and 10 of 91 (11%) cefaclor-treated patients. Thus, in these clinical trials cefprozil was shown to be a safe, well-tolerated and effective treatment for episodes of bronchitis in elderly patients.

Cefprozil is a new oral cephalosporin that has antimicrobial activity against the most common bacterial pathogens associated with bronchitis in the elderly.[1,2] These organisms include *Streptococcus pneumoniae* (pneumococcus), *Haemophilus influenzae*, *Moraxella (Branhamella) catarrhalis*, *Klebsiella pneumoniae* and *Staphylococcus aureus*. *Mycoplasma pneumoniae* infections are less common in elderly patients,[3] and the role of *Chlamydia pneumoniae* in this population is unknown.

The present study compares the results of treatment with cefprozil vs that with cefaclor in patients aged 65 years or older who had episodes of acute bronchitis or exacerbations of chronic bronchitis. The study participants included elderly patients from previously reported cases in which a bacterial pathogen was isolated from pretreatment sputum cultures,[2,4,5] as well as previously unreported cases of bronchitis in elderly patients. In the latter group, no bacterial pathogen had been identified in pretreatment cultures, but clinical signs and symp-
toms consistent with infectious bronchitis were present. Patients without pretreatment pathogens were treated empirically with either cefprozil or cefaclor, and the clinical response was determined.

Patients and Methods

Study Design

The study was a nonblinded, randomised clinical trial designed to compare the clinical efficacy and safety of cefprozil with that of cefaclor in elderly patients with mild to moderate bronchitis.

There were 30 investigators and study sites in Europe and North America (see list of investigators at end of paper). At each centre, patients were randomly selected to receive either cefprozil or cefaclor in a 2:1 (cefprozil:cefaclor) ratio in Europe and a 1:1 ratio in North America. Computer-generated randomisation schedules were provided by Bristol-Myers Squibb to each investigator, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

The protocol was reviewed and approved by an Institutional Review Board and informed consent was obtained from all patients, using a form that complied with United States Food and Drug Administration guidelines.

Patient Selection

Men and women 65 years of age or older were eligible if they presented with clinical signs and symptoms consistent with a mild to moderate bronchitis. Hospitalised patients were eligible if the investigator judged that the patient’s clinical infection could be appropriately treated with an oral agent.

Patients were excluded if they had had a serious reaction to a cephalosporin or penicillin, had used a long-acting parenteral penicillin within 2 weeks before enrolment, or were likely to receive other antimicrobial drugs concomitantly. Also excluded were patients with pre-existing medical conditions that might preclude administration of oral medications, such as renal or hepatic dysfunction, or malabsorption or other gastrointestinal disturbances.

Patients with severe respiratory tract infection that might require parenteral or chronic antibiotic therapy were not considered. Patients previously enrolled in the study were also excluded, as were those who had a disease that, in the opinion of the principal investigator, might influence the outcome of the treatment or mimic or complicate both the course and the evaluation of the infectious process, such as pulmonary malignancy, collagen disease, sarcoidosis, sickle cell disease or advanced chronic obstructive pulmonary disease.

Treatment

Cefprozil, supplied by Bristol-Myers Squibb, was administered orally at a dose of 500mg (two 250mg capsules) every 12 hours for a recommended treatment duration of 10 days. Cefprozil was taken without regard to food intake. Cefaclor, also supplied by Bristol-Myers Squibb, was administered orally at a dose of 500mg (two 250mg capsules) every 8 hours for a recommended treatment duration of 10 days.

Participants treated as outpatients were asked to complete a diary of treatment and were asked to return unused medication at the end of treatment to verify compliance with study drug administration. Concomitant medications, other than systemic antimicrobials, were allowed as clinically indicated.

Investigators were permitted to discontinue the study drug prematurely and remove the patient from the study if no pathogen was isolated from the pretreatment culture or if the isolated pathogens were resistant to either cefprozil or cefaclor. Early withdrawal was also allowed if there was a poor clinical response within 72 hours, intercurrent illness or serious adverse clinical events, or if the patient or investigator chose to withdraw.

Study Parameters

Within 48 hours before treatment, all patients completed a medical history, a clinical evaluation with documentation of signs and symptoms of infection, and a physical examination. A chest x-ray was performed within 72 hours before or within 48