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Letters to the Editor

Cefuroxime Efficacy in Treatment of Bacteremic Pneumonia Due to Penicillin-Resistant and Cefuroxime-Resistant *Streptococcus pneumoniae*

Because of treatment failure with the use of third-generation cephalosporins for penicillin-resistant pneumococcal meningitis, the National Committee for Clinical Laboratory Standards (NCCLS) amended the resistance interpretive criteria for *Streptococcus pneumoniae* (7). According to the 1993 criteria, strains for which the cefuroxime sodium MIC is ≥2 μg/ml are considered resistant. The newest recommendations by the NCCLS (8), based on Jorgensen et al. (5), do not specify modifications for cefuroxime sodium.

Penicillin-resistant pneumococcal pneumonia does not raise as serious a problem as meningitis does. High-dose penicillin G is effective against resistant strains for which penicillin MICs are up to 2 μg/ml, and ceftriaxone or cefotaxime may be useful when the penicillin MIC is higher (10). However, despite these recent suggestions, appropriate guidelines for the management of this infection with penicillin or other β-lactams have not been established.

Second-generation cephalosporins are recommended for the initial management of community-acquired pneumonia with comorbidity or for patients ≥60 years of age (9), and cefuroxime has been suggested recently as empiric therapy for acute human immunodeficiency virus (HIV)-associated bacterial pneumonia (1). Nevertheless, reports of cefuroxime therapy for penicillin-resistant pneumococcal pneumonia are very limited, and they do not include cefuroxime-resistant cases (12). This report is our experience with cefuroxime sodium in the treatment of bacteremic pneumococcal pneumonia caused by penicillin- and cefuroxime-resistant strains.

Among the patients with serious *S. pneumoniae* infections diagnosed during the last 5 years in our hospital, we identified 21 penicillin- and cefuroxime-resistant pneumococcal strains. MICs were determined by using the agar-dilution method. Three of these 21 strains were isolated from blood cultures of patients with community-acquired pneumonia who received intravenous cefuroxime sodium as therapy.

The characteristics of these three patients, the MICs of β-lactam antibiotics, treatment, and outcome are summarized in Table 1. One patient, who received 750 mg of cefuroxime sodium every 8 h, became afebrile but continued to have a cough and purulent sputum, and there were no changes in the radiological infiltrate on the 11th day. Then the treatment was switched to oral erythromycin with cure of the pneumonia. The other two patients, who received cefuroxime sodium at a dose of 1,500 mg every 8 h, followed by cefuroxime axetil, were cured.

Several arguments support the efficacy of cefuroxime sodium in the therapy of bacteremic pneumonia due to pneumococcal strains with decreased susceptibilty to cefuroxime. Cefuroxime has shown bactericidal activity in vitro against pneumococcal isolates for which cefuroxime MICs were up to 4 μg/ml (6). Levels in serum and lung tissue that can be achieved with intravenous cefuroxime are well above the MICs for our resistant strains. After an intravenous dose of 1 g, the mean peak concentration was 99.2 μg/ml and the serum cefuroxime concentration was greater than 6.25 μg/ml over a period of 180.7 min (3). Likewise, after intravenous doses of 750 and 1,500 mg of cefuroxime, the mean trough concentrations were 3.1 and 7.3 μg/ml, respectively (2). Moreover, it has been demonstrated that the most important pharmacokinetic parameter for the killing effect of cephalosporins in vivo is the time above MIC (4). Finally, levels in lung tissue of 17.1 μg/ml at 1 h and 14.7 μg/ml at 2 h have been attained after 750 mg of intravenous cefuroxime (11).

This preliminary experience suggests that intravenous cefuroxime, at a dose of 1,500 mg every 8 h, is effective therapy for bacteremic pneumococcal pneumonia due to penicillin- and cefuroxime-resistant strains, at least for strains with cefuroxime MICs of up to 4 μg/ml. Therefore, the present definition of cefuroxime sodium resistance for *S. pneumoniae* appears to be of uncertain clinical relevance.

TABLE 1. Characteristics of isolates and patients with pneumonia and pneumococcal bacteremia treated with cefuroxime sodium[a]

Patient no. (sex, age in yr)	Underlying disease	X-ray finding	Serotype	MIC (μg/ml)				Treatment	Outcome with
				P	CRM	CFT	CAX		
1 (male, 63)	Multiple myeloma	LUL alveolar infiltrate	9	0.5	2	0.25	1	CRM-iv, 750 mg q8h, 11d plus E-o, 500 mg q6h, 7d	Improvement
2 (male, 16)	HIV infection	LLL alveolar infiltrate	14	2	2	0.5	1	CRM-iv, 1,500 mg q8h, 6d plus CRM-o, 500 mg q12h 8d	Cure
3 (male, 69)	None	LLL alveolar infiltrate	14	2	4	0.5	1	CRM-iv, 1,500 mg q8h, 6d plus CRM-o, 500 mg q12h, 6d	Cure

[a] Abbreviations: LUL, left upper lobe; LLL, left lower lobe; CRM-iv, cefuroxime sodium intravenously; E-o, erythromycin orally; CRM-o, cefuroxime axetil orally; P, penicillin; CRM, cefuroxime; CAX, ceftriaxone.

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