JOURNAL OF CLINICAL MICROBIOLOGY, Dec. 1997, p. 3323–3324 Vol. 35, No. 12
0095-1137/97/$04.00+0

Susceptibilities of *Chryseobacterium indologenes* and *Chryseobacterium meningosepticum* to Cefepime and Cefpirome

PO-REN HSUEH,[1,2] LEE-JENE TENG,[2,3] PAN-CHYR YANG,[2] SHEN-WU HO,[2,3] AND KWEN-TAY LUH[1,2]*

Departments of Laboratory Medicine[1] and Internal Medicine,[2] National Taiwan University Hospital, and Department of Medical Technology, National Taiwan University College of Medicine,[3] Taipei, Taiwan

Received 2 September 1997/Returned for modification 16 September 1997/Accepted 26 September 1997

In vitro activities of cefepime and cefpirome against 96 isolates of *Chryseobacterium indologenes* and 21 of *C. meningosepticum* were determined by the agar dilution method. Overall, cefepime was more active than cefpirome against *C. indologenes* (MIC at which 50% of the isolates were inhibited [MIC_{50}] and MIC_{90}, 4 and 16 μg/ml, respectively, for cefepime and 8 and 128 μg/ml, respectively, for cefpirome). Both agents had poor potency against *C. meningosepticum* (MIC_{50} and MIC_{90}, 64 and >256 μg/ml, respectively, for cefepime and 128 and >256 μg/ml, respectively, for cefpirome).

Strains of *Chryseobacterium* species, including *Chryseobacterium indologenes* and *C. meningosepticum*, have been documented as human pathogens causing a variety of invasive infections, especially in hospitalized patients with severe underlying diseases who had indwelling devices implanted (3–6, 11). Appropriate choice of effective antimicrobial agents for treatment of infections caused by *Chryseobacterium* species is difficult because of the unpredictability and breadth of antimicrobial resistance of these organisms (1, 10). The "fourth-generation" cephalosporins (especially cefepime and cefpirome) have been demonstrated to have improved activity against a wide array of gram-positive and gram-negative bacteria, including nonfermentative gram-negative bacilli (2, 7, 9, 12). However, data on the susceptibility of *Chryseobacterium* species to fourth-generation cephalosporins are limited (7).

Ninety-six isolates of *C. indologenes* and 21 of *C. meningosepticum* recovered from various clinical specimens of 117 patients seen from January 1992 to June 1997 at the National Taiwan University Hospital were studied. These strains were identified in accordance with previous descriptions (4). MICs for these isolates were determined by the agar dilution method by following National Committee for Clinical Laboratory Standards guidelines (8) and using Mueller-Hinton agar (BBL Microbiology Systems, Cockeysville, Md.) and a multipoint inoculator with an inoculum of 10^4 CFU per spot. Powdered cefepime with known potency was kindly provided by Bristol-Myers Squibb Laboratories (Princeton, N.J.), and powdered cefpirome was provided by Hoechst Marion Roussel (Frankfurt, Germany). Concentrations of the two drugs ranged from 0.03 to 256 μg/ml. Plates were incubated at 35°C in ambient air, and MICs were read at 16 to 18 h.

The MICs of cefepime and cefpirome for five control strains were as follows: 0.03 and 0.06 μg/ml, respectively, for *Escherichia coli* ATCC 25922; 2 and 2 μg/ml, respectively, for *Pseudomonas aeruginosa* ATCC 27853; 2 and 1 μg/ml, respectively, for *Staphylococcus aureus* ATCC 29213; 0.5 and 0.25 μg/ml, respectively, for *C. indologenes* ATCC 29879; and 64 and 128 μg/ml, respectively, for *C. meningosepticum* ATCC 13253.

Table 1 shows data on the susceptibility of *Chryseobacterium* isolates to cefepime and cefpirome. Cefepime and cefpirome both had poor activity against isolates of *C. meningosepticum*. For *C. indologenes* isolates, cefpirome was less active, with MICs for 50 and 90% of the strains tested (MIC_{50} and MIC_{90}) that were twofold and eightfold, respectively, higher than those of cefepime. When we applied the cefepime MIC breakpoints for organisms other than *Haemophilus* species, *Neisseria gonorrhoeae*, and *Streptococcus* species published by the National Committee for Clinical Laboratory Standards in M7-A4 of January 1997 (≤8 μg/ml, susceptible; 16 μg/ml, intermediate; ≥32 μg/ml, resistant) to those of cefepime and cefpirome against *Chryseobacterium* species (8), the susceptibilities of *C. indologenes* to cefepime and cefpirome were 73 and 64%, respectively.

The MICs obtained in the present study and those in our previous report (1) were compared, although some subtle differences in the MICs due to technical differences may exist because the two testings were performed at different times. Except for piperacillin, all of the extended-spectrum β-lactam antibiotics tested had poor activity against strains of *C. meningosepticum* (1). Unfortunately, *C. meningosepticum* is a well-documented human pathogen causing severe infections, including meningitis, bacteremia, and catheter-related sepsis, complicating therapy especially in debilitated patients (11). For *C. indologenes* isolates, cefepime was the most active agent among the eight β-lactam antibiotics tested, although the potency of these agents was not satisfactory. However, for treating infections caused by *C. indologenes*, the most commonly encountered *Chryseobacterium* species, piperacillin, ceftazidime, cefoperazone, and fourth-generation cephalosporins may be considered the drugs of choice (1, 11).

Compared with expanded-spectrum cephalosporin susceptibility results for *C. indologenes* isolates tested previously (1), the MIC_{50} or MIC_{90} of cefepime was 1 $\log_2$ dilution lower than that of ceftazidime and 8 or more $\log_2$ dilutions lower than that of cefotaxime. The activity of cefpirome was equal to that of ceftazidime. Activities of cefepime and cefpirome against the *C. indologenes* isolates tested were approximately equal to those against *P. aeruginosa* (MIC_{50} and MIC_{90}, 4 and 32 μg/ml, respectively, for cefepime and 2 and 128 μg/ml, respectively, for cefpirome) (2, 7, 12). Also, more than 90% of the isolates of *C. indologenes* and *C. meningosepticum* with intermediate or complete resistance to ceftazidime showed cross-resistance to cefepime or cefpirome. These findings were in accord with previous descriptions of *P. aeruginosa* (12). The possibility of the presence of a novel β-lactamase such as an OXA-1-like

* Corresponding author. Mailing address: Department of Laboratory Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei, Taiwan. Phone: 886-2-3562150. Fax: 886-2-3224263.

TABLE 1. Antimicrobial susceptibilities of *C. indologenes* and *C. meningosepticum* to cefepime and cefpirome by the agar dilution method

Organism (no. of strains tested) and antimicrobial agent	MIC (μg/ml)			No. (%) of susceptible isolates
	Range	50% of isolates	90% of isolates	
C. indologenes (96)				
Cefepime	0.25–>256	4	16	70 (73)
Cefpirome	0.25–>256	8	128	61 (64)
C. meningosepticum (21)				
Cefepime	0.5–>256	64	>256	4 (19)
Cefpirome	1–>256	128	>256	4 (19)

β-lactamase, SHV-2 to SHV-6, and some extended TEM β-lactamases in *Chryseobacterium* isolates, like those of *Enterobacteriaceae* and *P. aeruginosa*, may contribute to this phenomenon and needs further investigation (12).

In summary, cefepime was more active than cefpirome against the *C. indologenes* strains tested. Both cefepime and cefpirome had poor activity against *C. meningosepticum* strains. For treating infections caused by *Chryseobacterium* species, determination of the MIC for each individual isolate is mandatory.

REFERENCES

1. **Chang, J. C., P. R. Hsueh, J. J. Wu, S. W. Ho, W. C. Hsieh, and K. T. Luh.** 1997. Antimicrobial susceptibility of flavobacteria determined by agar dilution and disk diffusion methods. Antimicrob. Agents Chemother. **41:**1301–1306.
2. **Fuchs, P. C., R. N. Jones, A. L. Barry, and C. Thornsberry.** 1985. Evaluation of the in vitro activity of BMY-28214, a new broad-spectrum cephalosporin. Antimicrob. Agents Chemother. **27:**679–682.
3. **Hsueh, P. R., T. R. Hsiue, and W. C. Hsieh.** 1996. Pyomyositis in intravenous drug abusers: report of a unique case and review of the literature. Clin. Infect. Dis. **22:**858–860.
4. **Hsueh, P. R., L. J. Teng, S. W. Ho, W. C. Hsieh, and K. T. Luh.** 1996. Clinical and microbiological characteristics of *Flavobacterium indologenes* infections associated with indwelling devices. J. Clin. Microbiol. **34:**1908–1913.
5. **Hsueh, P. R., T. R. Hsiue, J. J. Wu, L. J. Teng, S. W. Ho, W. C. Hsieh, and K. T. Luh.** 1996. *Flavobacterium indologenes* bacteremia: clinical and microbiological characteristics. Clin. Infect. Dis. **23:**550–555.
6. **Hsueh, P. R., L. J. Teng, S. W. Ho, W. C. Hsieh, and K. T. Luh.** 1997. Increasing incidence of nosocomial infections caused by *Chryseobacterium indologenes*. Eur. J. Clin. Microbiol. Infect. Dis. **16:**568–574.
7. **Jones, R. N., M. A. Lfaller, S. D. Allen, E. H. Gerlach, P. C. Fuchs, and K. E. Aldridge.** 1991. Antimicrobial activity of cefpirome: an update compared to five third-generation cephalosporins against nearly 6000 recent clinical isolates from five medical centers. Diagn. Microbiol. Infect. Dis. **14:**361–364.
8. **National Committee for Clinical Laboratory Standards.** 1997. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Approved standard M7-A4. National Committee for Clinical Laboratory Standards, Villanova, Pa.
9. **Sanders, C. C.** 1996. In vitro activity of fourth generation cephalosporins against *Enterobacteriaceae* producing extended-spectrum β-lactamases. J. Chemother. **8:**(suppl 2)**:**57–62.
10. **von Graevenitz, A., and M. Grehn.** 1977. Susceptibility studies of *Flavobacterium* II-b. FEMS Microbiol. Lett. **2:**289–292.
11. **von Graevenitz, A.** 1995. Nonfermentative gram-negative bacteria, p. 520–532. *In* P. R. Murray, E. J. Barron, M. A. Pfaller, F. C. Tenover, and R. H. Yolken (ed.), Manual of clinical microbiology, 6th ed. American Society for Microbiology, Washington, D.C.
12. **Watanabe, N. A.** 1996. Newer antipseudomonal cephalosporins. J. Chemother. **8**(Suppl. 2)**:**48–56.