Comparative Evaluation of Penicillin, Ampicillin, and Imipenem MICs and Susceptibility Breakpoints for Vancomycin-Susceptible and Vancomycin-Resistant Enterococcus faecalis and Enterococcus faecium

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Although imipenem has in vitro activity against Enterococcus faecalis and Food and Drug Administration-approved indications for treatment of infections caused by this microorganism, there are no NCCLS guidelines for susceptibility testing of imipenem versus enterococci. Therefore, the in vitro activities of penicillin, ampicillin, imipenem, and vancomycin against 201 blood isolates of E. faecalis and 24 blood isolates of Enterococcus faecium were compared. The susceptibility of isolates to penicillin or ampicillin accurately predicted the in vitro activity of imipenem. Since the susceptibility of enterococci to imipenem can be predicted by the results obtained by testing of penicillin or ampicillin, testing of imipenem by clinical laboratories probably is not necessary.

Imipenem, the first widely used carbapenem antimicrobial agent, was shown in early studies to have good in vitro activity against Enterococcus faecalis (1, 4, 5, 9, 10) but little activity against Enterococcus faecium (2). However, present NCCLS-approved standards for in vitro susceptibility testing (6, 7) provide no guidance for testing imipenem versus enterococci, nor are there statements in in vitro susceptibility results for other antimicrobial agents can predict the in vitro activity of imipenem against these bacteria. Nevertheless, clinicians and microbiologists attending a recent meeting of the NCCLS Subcommittee on Antimicrobial Susceptibility Testing (June 1999) agreed that penicillin and/or ampicillin treatment likely would predict the activity of imipenem (M. P. Weinstein, personal observation). In the absence of systematically gathered and published data, however, the question remains open. Therefore, 225 isolates from patients with enterococcal bacteremia were tested against imipenem, penicillin, ampicillin, and vancomycin to determine the in vitro activity of each agent as well as the degree to which each drug predicted the in vitro activity of imipenem.

Enterococcal isolates causing bacteremia in patients hospitalized at Robert Wood Johnson University Hospital from July 1997 through October 1999 were tested. These included 201 E. faecalis (24 vancomycin-resistant) and 24 E. faecium (19 vancomycin-resistant) isolates. All isolates were identified in the Robert Wood Johnson University Hospital Clinical Microbiology Laboratory using dried-overnight (conventional) gram-positive combination panels in the MicroScan WalkAway 96 Instrument (Dade MicroScan, Inc., West Sacramento, Calif.). Species identification of strains with unusual susceptibility patterns (e.g., vancomycin-intermediate E. faecalis and ampicillin-susceptible E. faecium) was confirmed by conventional microbiological testing (3). Prior to testing, isolates were thawed and subcultured twice to ensure purity and viability.

Each isolate was tested versus penicillin, ampicillin, imipenem, and vancomycin. Solutions of all antimicrobials were prepared from standard powders of known potencies obtained either from the manufacturer of the compound or from a commercial source (Sigma, St. Louis, Mo.). MICs were determined in duplicate by the microdilution method of the NCCLS using cation-adjusted Mueller-Hinton broth (7).

Of the 201 E. faecalis strains tested, 175 were susceptible to vancomycin (MIC ≤ 4 μg/ml), 2 were intermediate (MIC = 8 μg/ml for both strains), and 24 were resistant (MIC ≥ 32 μg/ml). The MIC ranges, MICs at which 50% of the isolates tested were inhibited (MIC₅₀), and MIC₉₀ of penicillin, ampicillin, and imipenem were comparable for vancomycin-susceptible and vancomycin-resistant isolates (Table 1). The MIC₉₀ of all three agents were in the susceptible range even for the vancomycin-resistant isolates. Of the 24 E. faecium strains tested, 5 were susceptible to vancomycin and 19 were resistant to vancomycin. The penicillin, ampicillin, and imipenem MIC ranges were of 64 μg/ml (Table 1).

Using the present published NCCLS breakpoints for penicillin and ampicillin versus enterococci (7) (susceptible, ≤8 μg/ml; resistant, ≥16 μg/ml) and the breakpoints for imipenem published in the manufacturer’s package insert approved by the Food and Drug Administration (FDA) (susceptible, ≤ 4 μg/ml; intermediate, 8 μg/ml; resistant, ≥16 μg/ml), the ability of penicillin and ampicillin MICs to predict in vitro susceptibility of enterococci versus imipenem was assessed. As shown in Table 2, of the 201 E. faecalis strains tested, penicillin results...
For imipenem against enterococci (6, 7) and, based on the data from this study, specific testing guidelines for imipenem do not appear to be needed. However, several limitations of the data make firm conclusions from this report problematic. First, all of the microorganisms tested came from a single institution. Second, a relatively small number of E. faecium strains were tested. Although it is possible that these strains might represent only a few clones, prior work from our institution has shown our E. faecium strains to be polyclonal (H. Soliman, K. L. Joho, K. Damerau, R. Kuk, M. P. Weinstein, and J. F. John, Abstr. 93rd Gen. Meet. Am. Soc. Microbiol. 1993, abstr. A-80, p. 15, 1993). Third, no species other than E. faecalis and E. faecium were included.

To address these limitations, it will be necessary to study additional E. faecalis and E. faecium strains from other geographic regions and, if possible, to include less common enterococcal species, such as Enterococcus gallinarum, Enterococcus casseliflavus, Enterococcus raffinosus, and Enterococcus avium, thereby meeting the suggested criteria of the NCCLS (8). If the initial results from the present study are confirmed, microbiology laboratories and clinicians will benefit from a therapeutic note in the NCCLS guidelines and tables indicating that the in vitro results obtained for penicillin or ampicillin will accurately predict the in vitro susceptibility of imipenem.

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REFERENCES


