concentration of antibiotic killing at least 99.9% of the initial bacterial inoculum.

The Table shows the MIC and MBC values of benzylpenicillin, ampicillin, cefditoren, cefotaxime, ceftriaxone and meropenem against the strains of *S. pneumoniae*, *H. influenzae* and *N. meningitidis*. For *S. pneumoniae* isolates the corresponding values for vancomycin are also included.

The most active in-vitro antibiotics against *S. pneumoniae* were cefditoren, ceftriaxone, cefotaxime and meropenem. Strains with diminished susceptibility or resistance to penicillin were less susceptible to the other β-lactam compounds but the MIC and MBC values for cefditoren were not higher than 1 and 2 mg/L for isolates resistant to penicillin (MIC and MBC values for penicillin up to 4 mg/L). All antibiotics tested were bactericidal. Vancomycin was equally active in vitro against all *S. pneumoniae* strains independently of their susceptibility to penicillin, and was also highly bactericidal against this pathogen.

The most active antibiotics against *H. influenzae* were cefditoren, ceftriaxone, cefotaxime and meropenem. Strains with diminished susceptibility or resistant to penicillin and ampicillin had MIC and MBC values for the other β-lactam antibiotics very similar to those for penicillin-susceptible strains. These results were probably related to the production of β-lactamase which affected only penicillin and ampicillin but not the cephalosporins or meropenem.

The most active compounds against *N. meningitidis* were ceftriaxone, cefditoren, cefotaxime and meropenem. Strains with diminished susceptibility to penicillin were less susceptible to the other β-lactam compounds than those fully susceptible to penicillin. Nevertheless, the MIC and MBC values of cefditoren were 7 to 30 times lower than the corresponding values for penicillin and very close to those of ceftriaxone and cefotaxime. All the *H. influenzae* and *N. meningitidis* strains studied, including those with diminished susceptibility or resistant to penicillin, were inhibited by 0.03 mg/L of cefditoren. On the other hand, 1 mg/L of cefditoren inhibited all *S. pneumoniae* strains, thus this antibiotic was as active as ceftriaxone and meropenem and slightly more active than cefotaxime. The bactericidal activity of cefditoren was very marked with MBCs 100% of 0.12 mg/L (*H. influenzae*) and 0.03 mg/L (*N. meningitidis*). The corresponding value for *S. pneumoniae* was 2 mg/L, an in-vitro activity similar to that of ceftriaxone, cefotaxime and meropenem.

Results previously published on the activity of cefditoren against penicillin-sensitive *S. pneumoniae* strains showed MICs 90% ranging from ≤0.025 to 0.78 mg/L (Tamura et al., 1988; Miyazaki et al., 1991) but there are few data on its activity against penicillin-resistant strains. Our results with *H. influenzae* show that cefditoren is equally active against strains with different degrees of penicillin susceptibility as previously published (Tamura et al., 1988; Miyazaki et al., 1991). We have not found any previous report on the activity of cefditoren against *N. meningitidis*, which we have shown is highly sensitive to cefditoren.

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References


Cystitis due to vancomycin-intermediate *Staphylococcus saprophyticus*  

Sir,

Coagulase-negative staphylococci (CNS) were universally susceptible to vancomycin. However, in the last decade, a few strains either resistant or of intermediate sensitivity to vancomycin have been reported (Veatch et al., 1990; Sanjay et al., 1991; Archer & Climo, 1994). This resistance to vancomycin is
alarming, since there is a potential cross-transmission of this resistance to other Gram-positive bacteria.

A 25-year-old Haitian woman without any previous medical history, presented to the outpatient clinic of our hospital complaining of diffuse lower abdominal pain. Urine analysis was abnormal showing numerous leucocytes and red blood cells. Urine culture taken before the administration of any antibiotics showed a pure growth of more than $10^4$ cfu/L of *Staphylococcus saprophyticus*. Bacterial identification was performed in our laboratory and confirmed at the Quebec Provincial Laboratory. Susceptibility testing was performed in our laboratory in duplicate, following the NCCLS recommendations, by an agar dilution method; the MIC for vancomycin was 8 mg/L. Susceptibility by a broth microdilution method, also done in duplicate at the Quebec Provincial Laboratory, gave the same result. Nevertheless, when testing vancomycin susceptibility by a disc diffusion method according to the NCCLS criteria (vancomycin disc 30 μg, Remel, Lenexa, KS, USA), the strain was found to be susceptible to vancomycin (zone diameters: 16 mm at the provincial laboratory, 17 mm in our laboratory). This strain was thus classified as of intermediate sensitivity to vancomycin, but was susceptible to oxacillin, erythromycin, clindamycin and trimethoprim-sulphamethoxazole. The patient was treated with the latter antibiotic. She unfortunately failed to return to her follow up visit and was lost to further follow up.

Vancomycin resistance among CNS has already been reported in *Staphylococcus haemolyticus* (Veach et al., 1990; Kloos & Bannerman, 1994) and in *Staphylococcus epidermidis* (Sanyal et al., 1991). However, this is to our knowledge, the first reported case of a *S. saprophyticus* strain of reduced sensitivity to vancomycin. Knowing that this microorganism is frequently implicated in urinary tract infections, this represents a worrying threat. We are witnessing an overall increase of resistance to vancomycin among CNS, and this could have a significant impact in clinical practice, with the increased importance of these organisms in nosocomial infections (Archer & Climo, 1994). An additional problem was the discrepancy observed between the disc diffusion and the serial dilution (agar and broth dilutions) methods of sensitivity testing. Considering serial dilution as the gold standard method, a major error was recorded with the disc diffusion method and this is worrying. The same problem has been noted previously by another group (Sanyal et al., 1991), although the Stokes’ method was used in that report. Clinical laboratories using disc diffusion, may have to revise their routine procedures when determining vancomycin susceptibilities of CNS.

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References


Pharmacokinetics of once-daily versus thrice daily tobramycin in cystic fibrosis patients


Sir,

Once-daily administration of aminoglycosides has been demonstrated to be as efficacious and no more toxic than traditional dosing in numerous clinical investigations (Preston & Briceand, 1995). Despite the presence of aminoglycoside levels above the minimum inhibitory concentration for only a fraction of the dosing interval, this method has been associated with a favourable outcome in most patients. In contrast with the above patient populations, the efficacy, pharmacokinetics, and toxicity of once-daily aminoglycosides has not been well studied in cystic fibrosis patients. It is well documented that cystic fibrosis patients have an altered pharmacokinetic disposition when compared to other patients. An increased volume of distribution and total body clearance have been observed, resulting in increased aminoglycoside requirements (deGroot & Smith, 1987). Some clinicians...