Importance of using current NCCLS breakpoints to interpret cefotaxime and ceftriaxone MICs for *Streptococcus pneumoniae*

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Sir,

In a recent article in this Journal, Caniça et al.1 reported *in vitro* activities for extended-spectrum cephalosporins tested against 384 isolates of *Streptococcus pneumoniae* with reduced susceptibility to penicillin. As the authors state, data such as these are essential because cefotaxime and ceftriaxone are important antimicrobial agents for the treatment of pneumococcal infections, and of particular importance for the treatment of patients with pneumococcal meningitis. Previous publications have reported that 1–3% of pneumococcal isolates submitted to clinical microbiology laboratories in the United States are from CSF specimens, compared with 97–99% of pneumococci from respiratory, blood and other specimen sources.2,3 Based on published studies, Caniça et al.1 noted that isolates of *S. pneumoniae* resistant to third-generation cephalosporins remain rare, whereas other investigators have observed that MIC distributions of third-generation cephalosporins are similar for meningeal and non-meningeal isolates of pneumococci.2 In those rare instances when third-generation cephalosporin-resistant pneumococci are isolated from patients’ CSF, alternative therapies should be prescribed.

In their paper, Caniça et al.1 emphasize the importance of pneumococcal meningitis, yet they do not analyse their data divided by meningeal and non-meningeal specimen sources (as suggested by the NCCLS4 presumably because very few isolates from CSF were actually collected, as has been observed previously.2,3 The authors determined MICs of cefotaxime and ceftriaxone using an NCCLS method and interpreted their results with NCCLS recommended breakpoints4 applicable to meningeal isolates (0.5 mg/L, susceptible; 1 mg/L, intermediate; 2 mg/L, resistant),4 of which their isolate collection undoubtedly contained very few such isolates. NCCLS breakpoints for cefotaxime, ceftriaxone and ceftipime for non-meningeal isolates of pneumococci were revised in 2002 from 0.5 mg/L (susceptible), 1 mg/L (intermediate) and 2 mg/L (resistant)5 to 1 mg/L (susceptible), 2 mg/L (intermediate) and 4 mg/L (resistant).4 Applying the updated NCCLS MIC interpretative breakpoints4 to this data set has a very dramatic impact on the perceived activities of cefotaxime and ceftriaxone against penicillin-intermediate and -resistant isolates of *S. pneumoniae*. If the MIC data in Table 1 of the Caniça et al.1 publication are studied, the following observations can be made. Of the penicillin-intermediate isolates, 97.7% were susceptible to cefotaxime and 99.0% were susceptible to ceftriaxone. The percentage of penicillin-resistant isolates intermediate to cefotaxime was actually 29.1% (23/79 isolates) and not 65.8% as reported by Caniça et al.1 Similarly, the percentage of penicillin-resistant isolates intermediate to cefotaxime was actually 8.9% (7/79) and not 83.6%. In addition, only 1.3% (1/79) of isolates resistant to penicillin were also resistant to cefotaxime or ceftriaxone, not 30.4% for cefotaxime and 10.1% for ceftriaxone as reported by Caniça et al.1 Almost every penicillin-susceptible isolate of *S. pneumoniae* (≥99.9%) has been previously reported to be susceptible to cefotaxime and ceftriaxone.2 Data published by the same laboratory in Portugal from an earlier study also need to be re-interpreted using the NCCLS M100-S12 breakpoints to determine whether changes in susceptibility to cefotaxime or ceftriaxone have actually occurred.7 Changes in the percentages of isolates interpreted as susceptible, intermediate and resistant can often mask important shifts in MIC distribution; monitoring shifts in MIC distribution can be a more sensitive method to identify changes in antimicrobial susceptibilities.

A common problem encountered by those who conduct and publish antimicrobial surveillance studies is that MIC breakpoints for some organism–antimicrobial combinations change frequently (e.g. *S. pneumoniae*), sometimes between the time a manuscript is submitted to and published by a peer-reviewed journal. This may have been the case for the recent paper by Caniça et al.1 but it is important to update incorrect data whenever possible so as not to mislead users of such data who may unintentionally apply it as printed. By using outdated MIC interpretative breakpoints, Caniça et al.1 have reported falsely high *S. pneumoniae* resistance rates for cefotaxime and ceftriaxone against penicillin non-susceptible isolates. In this time of increased resistance and limited...
choices of antimicrobial agents, reports of falsely high resistance rates can result in inappropriate use of agents, such as fluoroquinolones, when a β-lactam may be a more appropriate choice.

References


