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Prevalence of Antimicrobial Resistance among 723 Outpatient Clinical Isolates of Moraxella catarrhalis in the United States in 1994 and 1995: Results of a 30-Center National Surveillance Study

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Seven hundred twenty-three isolates of Moraxella catarrhalis obtained from outpatients with a variety of infections in 30 medical centers in the United States between 1 November 1994 and 30 April 1995 were characterized in a central laboratory. The overall rate of β-lactamase production was 95.3%. When the National Committee for Clinical Laboratory Standards MIC interpretive breakpoints for Haemophilus influenzae were applied, percentages of strains found to be susceptible to selected oral antimicrobial agents were as follows: azithromycin, clarithromycin, and erythromycin, 100%; tetracycline and chloramphenicol, 100%; amoxicillin-clavulanate, 100%; cefixime, 99.3%; cefpodoxime, 99.0%; cefaclor, 99.4%; loracarbef, 99.0%; cefuroxime, 98.5%; cefprozil, 94.3%; and trimethoprim-sulfamethoxazole, 93.5.

Moraxella catarrhalis is now recognized as a common cause of a variety of localized, community-acquired infections, in particular, acute otitis media, maxillary sinusitis, and acute purulent exacerbation of chronic bronchitis (3, 7, 10). Most clinical isolates of M. catarrhalis are found to produce one of two β-lactamas, BRO-1 and BRO-2 (5, 8, 11, 12). Both of these enzymes hydrolyze penicillin, ampicillin, and amoxicillin, although to differing degrees (i.e., BRO-1 hydrolyzes them to a greater extent than BRO-2) (5, 11). As a result, MICs of penicillin, ampicillin, and amoxicillin are elevated for β-lactamase-producing strains of M. catarrhalis, especially BRO-1 enzyme producers (1, 4, 6, 12). Whether production of either enzyme is associated with clinical failures in patients treated with these β-lactams has not been determined. Until such information is available, however, prudence would dictate that all infections caused by β-lactamase-producing M. catarrhalis, irrespective of which enzyme is produced, be considered refractile to management with penicillin, ampicillin, or amoxicillin.

Two recent large multicenter surveillance studies in the United States revealed overall rates of β-lactamase production of 84.1% in 1987 and 1988 (6) and 92.0% in 1992 and 1993 (1). Interestingly, there is some evidence that prior to 1976, in both the United States and Europe, M. catarrhalis rarely if ever produced β-lactamase (12).

Because the β-lactamas of M. catarrhalis are inhibited by clavulanate, the combination drug amoxicillin-clavulanate has been consistently active against this species (1, 4, 6). The same is true of oral cephalosporins, excepting cephalaxin and cefadroxil (4). Erythromycin and tetracycline resistance has been reported (2); however, the two most recent countrywide surveillance studies in the United States during 1987 and 1993 failed to identify a single macrolide- or tetracycline-resistant strain among a total of >1,000 isolates of M. catarrhalis. In contrast, trimethoprim-sulfamethoxazole (TMP-SMX) resistance is being reported with greater frequency (1).

The intent of the present study was to systematically determine the prevalence of antimicrobial resistance among current isolates of M. catarrhalis in the United States. Between 1 November 1994 and 30 April 1995, a total of 723 different isolates of this organism were prospectively collected from various specimens from outpatients in 30 different U.S. medical centers. For further characterization, isolates were transported to the University of Massachusetts Medical Center on rayon swabs immersed in 12 ml of Amies semisolid transport medium containing charcoal. Stock cultures were prepared with an absorbent-bead system (ProLab Diagnostics, Austin, Tex.), and organisms were stored at −70°C until further use. All organisms were subcultured twice on sheep blood agar plates prior to further characterization. Isolates were confirmed as M. catarrhalis on the basis of Gram stain morphology and production of oxidase and butyric acid esterase.

Susceptibility studies. MICs were determined by a broth microdilution procedure (100-μl total volume per well; final inoculum concentration, ca. 5 × 10^5 CFU/ml) in cation-adjusted Mueller-Hinton broth (Difco Laboratories, Detroit, Mich.), with trays incubated at 35°C in ambient air for 22 to 24 h prior to determination of results. Sixteen antibiotics, obtained from their respective manufacturers as laboratory-grade powders, were each tested in 12 different concentrations in an attempt to limit the number of off-scale results. The antimicrobial agents were penicillin, ampicillin, amoxicillin, amoxicillin-clavulanate (2:1), cefaclor, loracarbef, cefprozil, cefuroxime, cefixime, cefpodoxime, erythromycin, azithromycin, clarithromycin, TMP-SMX (1:19), chloramphenicol, and tetracycline. Staphylococcus aureus ATCC 29213 and Escherichia coli ATCC 25922 were used as controls. β-Lactamase production was assessed with all isolates by the nitrocefin disk assay (Cefinase; Becton Dickinson Microbiology Systems, Cockeysville, Md.). A total of 723 isolates of M. catarrhalis were characterized (mean number contributed per medical center = 24.1; range =
14 to 43). Males were the source of 57.2% of isolates. The percentages of isolates obtained from patients in different age groups were as follows: 0 to 5 years, 33.3%; 6 to 10 years, 4.8%; 11 to 20 years, 3.1%; 21 to 50 years, 18.2%; and >50 years, 40.6%. The percentages of isolates obtained from different specimens were as follows: middle ear fluid, 4.5%; sinus aspirates, 5.4%; conjunctival specimens, 7.4%; lower respiratory tract, 80.3%; blood, 1.7%; and other, 0.8%.

Of the 723 isolates, 689 (95.3%) produced β-lactamase. MIC results for 16 antimicrobial agents are listed in Table 1. MICs of all 10 β-lactam antimicrobial agents examined in this study were higher for β-lactamase-positive than for β-lactamase-negative strains. Overall, ampicillin was equivalent to amoxicillin in activity; both were more active than penicillin. The National Committee for Clinical Laboratory Standards (NCCLS) currently does not provide MIC interpretive breakpoints for β-lactam agents, threemacrolides(azithromycin, clarithromycin, and erythromycin), tetracycline, and chloramphenicol were uniformly active; all strains were susceptible. That was not true of TMP-SMX, to which only 93.5% of strains were susceptible. Taken collectively, the results of this surveillance study suggest that although rates of β-lactamase production have increased slightly, M. catarrhalis has not changed substantially in the context of antimicrobial resistance during the period since the last large U. S. multicenter surveillance study in 1992 and 1993 (3). A variety of oral antimicrobial agents remain suitable for the management of outpatient M. catarrhalis infections.

We thank Brendan Curley for technical assistance, Greg Giguere for statistical analysis, and Debbie McQuaid for excellent secretarial support. In addition, we thank the following individuals for provision of clinical isolates of M. catarrhalis: Melodie Beard, Rush-Presbyterian St. Luke’s Medical Center; Paul Bourbeau, Geisinger Medical Center; Joseph Campos, Children’s Hospital National Medical Center; Kimberly Chapin, University of South Alabama; Carla Clausen, Seattle Children’s Hospital; Frank Cockerill, Mayo Clinic; Judy Daly, Primary Children’s Medical Center; Gerald Dennis, Methodist Hospital; Phyllis Dell-Latta, Columbia Presbyterian Hospital; Michael Dunne, Henry Ford Hospital; Peter Gilligan, University of North Carolina.

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