Antimicrobial Susceptibilities of Group B Streptococci Isolated from Patients with Invasive Disease: 10-Year Perspective

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Antimicrobial susceptibility testing of 192 group B streptococcal isolates from patients with invasive disease demonstrated that 31 (16%) were resistant to erythromycin and 17 (9%) were resistant to clindamycin. One isolate demonstrated high-level resistance to streptomycin, but none was highly resistant to gentamicin. Erythromycin and clindamycin are no longer reliable empirical alternatives to penicillin for the treatment and prevention of group B streptococcal infections.

The group B streptococcus (GBS) is an important cause of neonatal sepsis and meningitis, infections in pregnant women, and invasive disease in nonpregnant adults, especially among those with diabetes mellitus, malignancy, liver disease, and other forms of immune impairment (2). Although GBS is regarded as uniformly susceptible to penicillin, recent reports have highlighted the emergence of strains resistant to erythromycin and clindamycin (3, 5, 6, 8–11). The presence of these resistant strains raises concerns about the use of erythromycin and clindamycin for the prophylaxis or treatment of GBS infections in patients allergic to β-lactams.

For serious GBS infections, an aminoglycoside is often administered in combination with penicillin or ampicillin to provide bactericidal synergism. Although rarely tested for, high-level aminoglycoside resistance, which indicates that the isolate will not be affected synergistically by a combination of a penicillin plus an aminoglycoside, has been documented in GBS isolates (1).

Therefore, we tested all strains of GBS isolated from patients with invasive disease at Duke University Medical Center over a 10-year period to determine the patterns of antimicrobial resistance, including high-level aminoglycoside resistance.

A total of 192 clinical isolates of GBS were studied. All isolates were obtained from the blood or cerebrospinal fluid of patients admitted to Duke University Medical Center between July 1990 and June 2000. The patients were 20 neonates with early-onset disease, 14 neonates with late-onset disease, 10 children, 2 pregnant women, and 146 nonpregnant adults. Identification of GBS was made by standard methods and latex agglutination (Streptex; Murex Biotech, Dartford, United Kingdom).

Susceptibility testing was performed by the broth microdilution method with cation-adjusted Mueller-Hinton broth supplemented with 2 to 5% lysed horse blood as recommended by the National Committee for Clinical Laboratory Standards (NCCLS) (7). The MICs of penicillin, ampicillin, ceftriaxone, clindamycin, erythromycin, vancomycin, levofloxacin, and chloramphenicol were determined as outlined by NCCLS; and the MIC of meropenem, which is used for the therapy of meningitis with penicillin-resistant Streptococcus pneumoniae, was determined as described previously (4). In addition, wells containing gentamicin and streptomycin at concentrations of 500, 1,000, and 2,000 μg/ml were used to detect the presence or absence of high-level aminoglycoside resistance. Preprepared microdilution trays, based on the MicroScan MICSTREP panel, were manufactured and provided by Dade Behring Inc. (West Sacramento, Calif.).

Frozen isolates of GBS were thawed, inoculated onto 5% sheep blood agar, and incubated at 35°C in an atmosphere containing 5% CO₂ for 18 to 24 h. Each isolate was subcultured onto fresh 5% sheep blood agar and incubated for an additional 18 to 24 h. Five to 10 colonies were then emulsified into 3 ml of deionized water to a turbidity equivalent to that of a 0.5 McFarland standard. The suspension in each well was then diluted to a final concentration of approximately 5 × 10⁵ CFU/ml. The microdilution trays were incubated in ambient air at 35°C for 20 to 24 h. S. pneumoniae ATCC 49619, Enterococcus faecalis ATCC 51299, and E. faecalis ATCC 29212 were used as controls. The MIC was defined as the lowest concentration of antibiotic that inhibited bacterial growth.

The susceptibilities of the 192 isolates to all antibiotics tested except gentamicin and streptomycin are summarized in Table 1. Thirty-one isolates were resistant to erythromycin (MICs, ≥1 μg/ml), 17 were resistant to clindamycin (MICs, ≥1 μg/ml), and 2 were resistant to chloramphenicol (MICs, ≥16 μg/ml). All but one of the clindamycin-resistant isolates were also resistant to erythromycin. The rates of resistance to both erythromycin and clindamycin increased over the 10-year study period. For the period from July 1990 to June 1995, 12% of isolates were resistant to erythromycin and 4% were resistant to clindamycin; from July 1995 to June 2000, the rates of erythromycin and clindamycin resistance had risen to 20 and 10%, respectively.

High-level resistance to gentamicin was not detected in any of the isolates, but for one isolate the streptomycin MIC was 1,000 μg/ml. The latter isolate was also notable for its reduced susceptibility to erythromycin (MIC, ≥64 μg/ml) and chloramphenicol (MIC, 16 μg/ml).

Our findings confirm those reported by other investigators. GBS strains isolated from patients with invasive disease remain uniformly susceptible to β-lactams, but resistance to erythro-
mycin and clindamycin has emerged to a clinically significant level. Other recent reports from North America have documented rates of erythromycin resistance of 6.7 to 21% and rates of clindamycin resistance of 3.4 to 15% (3, 5, 6, 8–10). Resistance rates are even higher in Taiwan, where 29.7% of isolates were highly resistant to clindamycin (11).

To our knowledge, this study is the first to systematically test for high-level aminoglycoside resistance in GBS isolates from North America. Only one isolate exhibited high-level resistance to streptomycin. This is in contrast to France, where more than 10% of GBS isolates were found to be highly resistant to streptomycin (1). None of our GBS isolates were highly resistant to gentamicin. To date, this type of resistance has been documented in only one GBS strain, which was isolated in Paris in 1987 (1).

Penicillins remain the preferred antibiotics for prophylaxis and treatment of GBS infections. Routine testing for susceptibilities to β-lactams and for high-level aminoglycoside resistance is unnecessary. However, erythromycin and clindamycin can no longer be considered reliable alternatives to β-lactams, and susceptibilities to these agents should be determined in the setting of penicillin intolerance.

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REFERENCES


