Fluoroquinolone-Resistant Group B Streptococci in Acute Exacerbation of Chronic Bronchitis

To the Editor: Fluoroquinolones (FQs) that are active against streptococcal species (e.g., levofloxacin and moxifloxacin) have been recommended by numerous national health authorities and international organizations for treating acute exacerbations of chronic bronchitis and pneumonia in adults (1). However, use of these antimicrobial drugs for treating community-acquired infections has led to an increase in FQ-resistant strains in bacteria such as Streptococcus pneumoniae. Group B streptococci (GBS, e.g., S. agalactiae) are the leading cause of invasive infections (pneumonia, septicemia, and meningitis) in neonates. GBS are also associated with bacteremia, endocarditis, and arthritis, and are responsible for deaths and illness in nonpregnant women with underlying diseases and in elderly adults (2). We describe, to our knowledge, the first GBS clinical isolate in France resistant to FQ; the isolate was from a patient treated with levofloxacin.

GBS CNR0717 strain was isolated as the predominant bacterium in a culture (>10^7 CFU/mL) from 2 purulent sputum samples from an 80-year-old man (leukocytes >25, epithelial cells <10) obtained 8 days apart. This patient was treated for 2 weeks with levofloxacin, 750 mg/day, for acute exacerbation of chronic bronchitis. No other relevant respiratory bacterial pathogens were present in these samples. GBS CNR0717, a capsular serotype IV strain, was suspected to have reduced susceptibility to FQs because no inhibition zone was observed around disks containing norfloxacin and pefloxacin disks, and reduced diameters were observed around disks containing ciprofloxacin and levofloxacin. Antibiograms were performed according to recommendations of the Clinical and Laboratory Standards Institute (3) on Mueller Hinton agar (Bio-Rad, Marnes la Coquette, France) supplemented with 5% horse blood. This strain was susceptible to all other antimicrobial drugs usually active against GBS (penicillin, erythromycin, clindamycin, tetracycline, rifampicin, vancomycin) and showed low-level resistance against aminoglycosides. MICs for 6 FQs (Table) indicate that GBS CNR0717 was highly resistant to pefloxacin and norfloxacin, with MICs >64 mg/L, and showed increased MICs for ciprofloxacin, sparflloxacin, levofloxacin, and moxifloxacin. No reduction of FQ MICs was observed with reserpine (10 mg/L), which indicated that resistance to FQ was not caused by an active efflux pump system.

Three major mutations have been reported for FQ resistance in streptococci at codon positions 81 in gyrA and 79 or 83 in parC (4). DNA sequence analysis of these regions showed a mutation in parC (Ser 79 → Tyr) but not in the wild-type susceptible strain (NEM316). No mutation was detected in the gyrA gene. FQ resistance in streptococci is acquired through a stepwise process and has been extensively studied in S. pneumoniae. First-step mutants conferring low-level resistance generally result from mutations in either gyrA or parC. There is also

Table. MICs of fluoroquinolones for strains of group B streptococci (GBS), France

<table>
<thead>
<tr>
<th>Strain</th>
<th>MIC (mg/L)*</th>
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<tbody>
<tr>
<td></td>
<td>Pef</td>
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<tr>
<td>GBS CNR0717</td>
<td>&gt;64</td>
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<tr>
<td>GBS NEM316</td>
<td>16</td>
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</tbody>
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*Pef, pefloxacin; Nor, norfloxacin; Cip, ciprofloxacin; Spa, sparflloxacin; Lev, levofloxacin; Mox, moxifloxacin.
a molecule-dependent target specificity: mutations in parC are generally selected by pefloxacin, ciprofloxacin, and levofloxacin, and those in gyrA are selected by sparfloxacin, gatifloxacin, moxifloxacin, gemifloxacin, and garenoxacin (5). In second-stage mutants, mutations are present in both parC and gyrA and confer resistance to the antistreptococcal FQs levofloxacin, moxifloxacin, and gatifloxacin.

FQ resistance in GBS has been reported in Japan, the United States, and Spain (6–8). Up to now, all FQ-resistant GBS strains described were highly resistant because of point mutations in gyrA and parC QRDR; a parC mutation at position 79 was present in all strains. These strains were isolated from elderly adults who, in some cases, had received quinolone therapy. Low-level resistance to FQ in GBS CNR0717 was associated with a Ser 79 → Tyr mutation in parC. Therefore, although the FQ sensitivity of this strain is unknown, a first-stage mutant could have been selected in vivo as our patient was treated with levofloxacin for 2 weeks.

GBS is an unusual cause of acute bacterial exacerbation of chronic bronchitis compared with other respiratory pathogens such as S. pneumoniae, but pathologies associated with this bacterium are changing. Clinical microbiologists should be aware of these changes and test isolates of Streptococcus spp. for susceptibility to FQs. This report indicates that FQ resistance among streptococci is a growing concern and that levofloxacin can select in vivo parC first-step mutants that will facilitate emergence of high-level FQ-resistant GBS strains, as demonstrated in vitro for S. pneumoniae (9). Finally, although FQ treatment is recommended for high-risk groups with acute exacerbations of chronic bronchitis, these antimicrobial drugs must be reserved for situations in which there are no effective alternative drugs to treat infections caused by multidrug-resistant bacteria. For susceptible strains, β-lactams, which still constitute the first-line recommended antimicrobial drugs, should be used for treatment of these patients (10).

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Dengue and Relative Bradycardia

To the Editor: In a recent letter to Emerging Infectious Diseases, Latteef and colleagues identified a relationship between dengue and relative bradycardia in patients in Singapore. They stated that “To our knowledge, this sign has not been previously associated with dengue” (1). Unfortunately, the association of dengue fever with relative bradycardia has already been well established and is certainly not a new finding (2,3). Despite this, however, there is no harm done in reinforcing an often forgotten clinical sign that can assist in the diagnosis of dengue, especially in those countries with limited resources.

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