Research letters

References


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First detection of plasmid-mediated quinolone resistance in the community setting and in hospitalized patients in Switzerland

Nadia Liassine1, Patricia Zulueta-Rodriguez2, Céline Corbel2, Christine Lascols2, Claude-James Soussy2,3 and Emmanuelle Cambau2,3*

1Unilabs Genève, Laboratoire de Microbiologie, Genève, Switzerland; 2Université Paris 12, IFR10, Créteil F-94010, France; 3AP-HP, Groupe Hospitalier Henri Mondor-Albert Chenevier, Bactériologie-Virologie-Hygiène, Créteil F-94010, France

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*Correspondence address: Bacteriologie, CHU Henri Mondor, 51 Avenue du Marechal de Lattre de Tassigny, 94010 Créteil Cedex, France. Tel: +33-149812831; Fax: +33-149812839; E-mail: emmanuelle.cambau@hmn.aphp.fr
†Present address: Dianalabs, 6 rue de la Colline, 1205 Genève, Switzerland.
‡Present address: Medicine Interne Department, Hospital Angeles del Pedregal, Mexico, D.F., Mexico.

Sir,

Plasmid-mediated quinolone resistance described so far is mainly due to qnr genes (qnrA, qnrB, qnrS and their variants).1 qnr-positive (qnr+) strains were isolated as early as 1994, but mainly from 2001 onwards in strains producing extended-spectrum β-lactamases (ESBLs).3 No strain has been reported to date in Switzerland, although ESBL-producing Enterobacteriaceae are prevalent and qnr+ isolates were reported in France and Germany, which border Switzerland.1,2 In contrast to previous prevalence studies that have been conducted in the hospital setting, we screened isolates from a non-hospital laboratory in Switzerland.

Non-duplicate ESBL-producing Enterobacteriaceae were consecutively isolated from April 2001 to February 2006 in Unilabs-Geneva Laboratory, the main laboratory serving both private practitioners and private clinics in the Geneva area comprising 400,000 inhabitants. qnr detection was performed by separate PCR amplifying qnrA, qnrB or qnrS as described previously.2,3 For qnr+ isolates, MICs of quinolones (Etest method), ESBL gene detection and fingerprinting were performed as described previously.2 The 155 isolates, tested mainly Escherichia coli (80%) and Klebsiella pneumoniae (14%), were from 87 (56.1%) outpatients and 68 (43.9%) inpatients with a mean age of 53 years (range: 1–92). Urinary tract infection (UTI) dominated in 129 cases (83.2%). The overall prevalence of ciprofloxacin resistance was 68% with no difference according to the origin of the patient (69% in outpatient versus 67% in inpatient, P = 0.7) or the year of isolation (data not shown).

The prevalence of qnr+ isolates was 2.6% with 1.5% (1/68) in hospitalized patients and 3.4% (3/87) in patients from the community setting. The four isolates were: two Citrobacter freundii with the qnrB4 allele, one K. pneumoniae with qnrB4 and one E. coli with qnrB2. Microbiological characteristics are described in Table 1. ESBL genes associated with qnr were blacTXM-15 (two isolates), blacTXM-3 (one isolate) and blacTXM-9 (one isolate). Of the four patients, three were cared by private physicians in the community setting. Patient 1 and Patient 2, who were both over 80 years old, were new cases of UTI, as far as we knew. Patient 1 originated from Libya and was visiting Geneva. Patient 2 was a Geneva inhabitant suffering from cystitis. In contrast, Patient 3, who had suffered from multiple urologic surgical interventions, and Patient 4, who was a paraplegic patient, presented recurrent UTIs. For Patient 3, an E. coli was found concomitantly to the qnrB4+ C. freundii in the urine specimen on early October 2005. This E. coli isolate, although negative for ESBL genes, harboured qnrB4 and bladMA1 encoding a plasmidic AmpC-type β-lactamase, an association originally described in K. pneumoniae. qnrB4 transfer between the two strains was unlikely since they did not share the same plasmid. In the urine sampled 5 days later (no. 1703), the E. coli qnrB4+ had disappeared and the C. freundii was alone. Since the second C. freundii isolate showed higher fluoroquinolone MIC than the C. freundii isolate 1696-1 and shared the same fingerprint, we sought for a mutation in the topoisoasmerases (gyrA, gyrB, parC and parE) in the latter isolate. Strikingly, a GyrA T83I modification was found in the two C. freundii isolates, which explained the MIC of 2 mg/L for the first C. freundii but did not explain the 4- to 10-fold difference in fluoroquinolone MICs between the two isolates.4 A recurrent infection diagnosed 8 months later was due to qnr-negative E. coli isolates, different in their ESBL gene content and associated resistances (Table 1). For Patient 4, the additional isolates collected 3, 6 and 9 months later than the qnrA-negative E. coli isolates, which explained the MIC of 2 mg/L for the first C. freundii but did not explain the 4- to 10-fold difference in fluoroquinolone MICs between the two isolates.4 A recurrent infection diagnosed 8 months later was due to qnr-negative E. coli isolates, different in their ESBL gene content and associated resistances (Table 1). For Patient 4, the additional isolates collected 3, 6 and 9 months later than the qnrB2+ isolate were qnr-negative and showed different fingerprints (data not shown), showing that the recurrent UTI episodes were related to re-infection and not to relapse.
Table 1. Microbiological data for patients with infections due to qnr strains

<table>
<thead>
<tr>
<th>Patient Age (years)/sex</th>
<th>Isolate no.</th>
<th>Specimen</th>
<th>Date</th>
<th>Species</th>
<th>Antimicrobial resistance</th>
<th>qnr allele</th>
<th>MIC (mg/L)</th>
<th>ESBL type</th>
<th>NAL</th>
<th>NOR</th>
<th>CIP</th>
<th>OFX</th>
<th>LVX</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 83/M</td>
<td>1173-1</td>
<td>urine</td>
<td>Jun 2004</td>
<td>C. freundii</td>
<td>AMP, CRO, GEN, TOB, SXT, CIP, FUR</td>
<td>qnrB4</td>
<td>32</td>
<td></td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>2 86/F</td>
<td>1640</td>
<td>urine</td>
<td>Sep 2005</td>
<td>p. pneumoniae</td>
<td>AMP, CRO, GEN, TOB, SXT, CIP, FOS, FOS</td>
<td>qnrB4</td>
<td>256</td>
<td></td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>3 2 8 2</td>
<td>CTX-M-9</td>
<td>E. coli</td>
<td>Dec 2005</td>
<td>E. coli</td>
<td>AMP, CRO, GEN, TOB</td>
<td>qnrB4</td>
<td>8</td>
<td>1</td>
<td>0.38</td>
<td>1.5</td>
<td>0.5</td>
<td>no ESBL</td>
<td></td>
</tr>
<tr>
<td>4 44/M</td>
<td>1696-2a</td>
<td>urine</td>
<td>Oct 2005</td>
<td>E. coli</td>
<td>AMP, CRO, GEN, TOB, SXT, CIP</td>
<td>qnrB4</td>
<td>169</td>
<td></td>
<td>32</td>
<td>32</td>
<td>32</td>
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</tr>
</tbody>
</table>

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To our knowledge, this is the first report of plasmid-mediated quinolone resistance from clinical isolates in Switzerland. In comparison with other studies, a low qnr prevalence was found and only concerned qnrB (no qnrA+ and qnrS+ isolates). This was not due to an epidemic phenomenon since isolates were distinct strains. First isolation of a qnr+ isolate was in June 2004. The clinical impact of qnr is unclear. The fact that for the two patients suffering from recurrent UTI Enterobacteriaceae strains isolated some months after the qnr+ strains did not contain qnr any more indicates that qnr may not bring advantage for colonization or infection.

Three qnr+ isolates were from outpatients and also harboured an ESBL gene of type CTX-M-15 or CTX-M-3 (Gly240Asp point mutant of CTX-M-15). A qnr+ isolate has been described once in an outpatient from Brazil and was also extensively described in Salmonella, which are typical community pathogens. In Switzerland, as in other countries, CTX-M-15 production is increasingly reported in isolates from the community. The possible dissemination of qnrB genes together with CTX-M genes requires our vigilance and highlights the necessity for all laboratories, even private laboratories, to detect accurately the presence of ESBL and qnr genes.

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Transparency declarations

None to declare.

References