A Fluoroquinolone-Resistant *Escherichia coli* Clinical Isolate without Quinolone Resistance-Determining Region Mutations Found in Japan

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A Fluoroquinolone-Resistant Escherichia coli Clinical Isolate without Quinolone Resistance-Determining Region Mutations Found in Japan

Fluoroquinolones are broad-spectrum and highly bactericidal antimicrobials agents that are used to treat various bacterial infections. Escherichia coli infections, especially in the urinary tract, are frequently treated with fluoroquinolones, and fluoroquinolone resistance has increased in the clinical field. Fluoroquinolone resistance is caused mainly by chromosomal mutations in the quinolone resistance-determining region (QRDR) of gyrA and gyrB, which encode DNA gyrase subunits, and parC and parE, which encode topoisomerase IV subunits. Moreover, plasmid-mediated quinolone resistance (PMQR) genes have been reported in Gram-negative bacteria, including E. coli. The acquisition of PMQR genes alone results in a low level of fluoroquinolone resistance and does not lead to MICs exceeding the breakpoints of these agents.

We isolated an E. coli strain, named HUE1, from the urinary catheter of a 77-year-old female patient in 2008 at Hokkaido University Hospital (Sapporo, Japan). The multilocus sequence type of this microorganism was ST171, and the phylogenetic group was A. The MICs of ciprofloxacin (CIP), levofloxacain (LVX), and nalidixic acid (NAL) exceeded the resistance breakpoints proposed by the Clinical and Laboratory Standards Institute (CLSI) (Table 1). The CLSI breakpoint for LVX is ≤2 μg/ml susceptible and ≥8 μg/ml resistant, that for CIP is ≤1 μg/ml susceptible and ≥4 μg/ml resistant, and that for NAL is ≤8 μg/ml susceptible and ≥32 μg/ml resistant (2). However, direct sequencing did not reveal any mutations in the QRDR of gyrA, parC, parE, or gyrB. We then screened for PMQR genes qnrS, qnrA, qnrB, qnrC, qnrD, aac(6′)-Ib-cr, qepA, and oqxAB by PCR. HUE1 was positive for qnrS and oqxAB (Table 1).

OqxAB is a new plasmid-encoded efflux pump belonging to the RND type and was first found in E. coli from swine manure in 2003 (6). It confers resistance to several antimicrobial agents, such as olaquindox, trimethoprim, and chloramphenicol, and a slight decrease in susceptibility to fluoroquinolones (3). Isolation of oqxAB-harboring Enterobacteriaceae has been reported only in Sweden and Denmark, South Korea, and China (3, 5, 7), and isolates derived from human patients have been reported only in South Korea. This letter provides the first report of oqxAB-harboring E. coli in Japan. Zhao et al. reported the isolation of E. coli harboring both qnrS and oqxAB from pigs in China (7). These isolates showed no mutations in the QRDR of gyrA and parE, however, mutations in that of parE and gyrB have not been determined. These isolates showed CIP MICs of 1 to 2 μg/ml, and they are therefore susceptible or intermediate according to the CLSI breakpoints.

OqxAB and QnrS increase the MIC of CIP approximately 32-fold and 64-fold, respectively (1, 5). These reports suggest that fluoroquinolone resistance in HUE1 without mutations in QRDR is caused by the concomitant presence of oqxAB and qnrS. However, other mechanisms may be associated with fluoroquinolone resistance in HUE1; therefore, further investigations are needed.

In conclusion, we present the first report of fluoroquinolone resistance in an E. coli isolate that is independent of mutations in the QRDR. The isolate harbored two PMQR genes, qnrS and oqxAB.

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<table>
<thead>
<tr>
<th>Strain</th>
<th>QRDR mutations</th>
<th>PCR</th>
<th>MIC (μg/ml)b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>gyrA parC parE gyrB</td>
<td>oqxAB oqxAB qnrS</td>
<td>ENR CIP LVX PUR STX NAL</td>
</tr>
<tr>
<td>HUE1</td>
<td>WT WT WT WT</td>
<td>+ + +</td>
<td>8 4 8 4 2 128</td>
</tr>
</tbody>
</table>

a WT, wild type.
b ENR, enrofloxacin; PUR, prulifloxacin; STX, sitafloxacin.
REFERENCES


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