Outbreak of OXY-2-Producing *Klebsiella oxytoca* in a Renal Transplant Unit

Mariela Soledad Zárate,1* Ana C. Gales,3 Renata C. Picão,3 Gervasio Soler Pujol,2 Alejandra Lanza,4 and Jorgelina Smayevsky1

Laboratorio de Bacteriología, Micología y Parasitología,1 Sección de Nefrología,2 Centro de Educación Médica e Investigaciones Clínicas Norberto Quiró (CEMIC), Ciudad Autónoma de Buenos Aires, Argentina, and Laboratorio ALERTA, Disciplina de Infectología, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil3

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We describe a *Klebsiella oxytoca* infection outbreak in a renal transplant unit that involved seven patients. All strains belonged to a single pulsed-field gel electrophoresis pattern and were resistant to amoxicillin-clavulanate, cefuroxime, pipercillin-tazobactam, and aztreonam but susceptible to ceftriaxone, ceftazidime, cefepime, and imipenem. Chromosomal β-lactamase hyperproduction was caused by a point mutation in the *bla*OXY-2 gene promoter region.

*Klebsiella oxytoca* is an opportunistic pathogen responsible for causing health care-associated infections (14, 15, 17). These species possess chromosomal genes encoding β-lactamases that are constitutively expressed at low levels and that confer resistance to amino- and carboxypenicillins but not to other β-lactams (4). *K. oxytoca* β-lactamases were initially divided into the two main groups OXY-1 and OXY-2, which possessed distinct β-lactam hydrolytic profiles (11, 12). Recently, other OXY-type β-lactamases (OXY-3 to OXY-6) have been reported among *K. oxytoca* isolates (6). Distinct point mutations in the −35 and −10 promoter regions of these β-lactamase genes have been pointed out as a reason for OXY hyperproduction in 10 to 20% of *K. oxytoca* isolates and led to a broader spectrum of β-lactam resistance (10, 13).

Susceptibility to bacterial infection in renal transplantation recipients is related directly to the level and duration of the pharmacological immunosuppression. Bacterial urinary tract infections are frequently associated with early onset chronic rejection and may lead to reduced transplantation survival (8).

*K. oxytoca* infection outbreaks have been documented in multiple settings (4, 15, 18, 19, 21). However, *K. oxytoca* infection outbreaks in transplantation units have not yet been reported. The aim of this study was to evaluate the antimicrobial susceptibility profiles, the genetic relatedness, and the mechanisms of β-lactam resistance among clinical isolates of *K. oxytoca* that caused health care-associated infections in a renal transplantation unit of a teaching hospital located in Buenos Aires, Argentina.

Seven *K. oxytoca* strains were isolated from the urine, peritoneal fluid, and central venous catheters of renal and renal-pancreas transplantation patients hospitalized at the transplantation unit of the University Hospital, CEMIC, between March and August of 2005. According to an epidemiological investigation, the index case was a renal transplantation patient who developed a urinary tract infection caused by this strain during the hospitalization period. The outbreak of infection involved a total of seven patients (one isolate per patient). Horizontal transmission was suspected because at that time, the transplantation unit was located in a shared facility without individual rooms, and all patients were attended by a common group of health care workers.

The isolates were associated with infection and were identified by conventional methods (5). Antimicrobial susceptibility testing was performed by using the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method and interpreted according to CLSI breakpoints (CLSI, 2006). Quality control was performed by testing *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. All quality control results were within published MIC ranges (CLSI, 2006) (2, 3). Pulsed-field gel electrophoresis (PFGE) was performed using the restriction endonuclease SpeI as previously described (16). Analysis of PFGE patterns was performed by visual inspection of photographs of ethidium bromide-stained gels. The isolates were classified according to the criteria described by Tenover et al. (20).

Detection of the *bla*OXY group genes and promoter regions was carried out by PCR, followed by DNA sequencing. PCR was performed under standard conditions, using the primers OXY-F (5′-GATTTCACAAAGCGCTGCGC-3′) and OXY-R (5′-CTGCTGGCCTGGGAGGAAA-3′), designed based on the nucleotide sequences of the *bla*OXY-1 and *bla*OXY-2 genes available at GenBank, under accession numbers Z30177 and Z49084, respectively. PCR products were analyzed by electrophoresis in 1.0% agarose gels and were sequenced on both strands by using an ABI Prism 377 sequencer unit. The nucleotide sequences and deduced amino acid sequences were analyzed by using Lasergene software (DNASTar, Madison, WI). The sequences obtained were compared to sequences available at http://www.ebi.ac.uk/ fasta33/.

The outer membrane proteins of the isolates were studied according to the method described by Filip et al. (7). Wild-type *K. oxytoca* strains susceptible to penicillins and broad-spectrum cephalosporins were included as control strains.

The antimicrobial susceptibility profiles of the *K. oxytoca* strains studied are presented in Table 1. The seven *K. oxytoca* strains...
were resistant to piperacillin, piperacillin-tazobactam, amoxicillin-clavulanic acid, cefuroxime, and aztreonam but were susceptible to ceftriaxone, ceftazidime, and cefepime, as observed with our study. This feature helps to distinguish OXY-type overproducers from other profiles displayed by clone A.

In summary, a unique clone of \textit{K. oxytoca} wild type carrying \textit{bla}_{\text{OXY-2}} was identified. The outer membrane profiles were identical among the \textit{K. oxytoca} isolates studied, except for the cefoxitin-resistant strain, which exhibited reduced expression of the 36-kDa outer membrane protein on a sodium dodecyl sulfate-polyacrylamide gel.

We describe an outbreak of \textit{K. oxytoca} infection among transplantation patients (hospitalized in a single institution), caused by an isolate that overproduces OXY-2 due to a mutation in the \textit{bla}_{\text{OXY-2}} promoter region. OXY-β-lactamases are chromosomally encoded and are usually synthesized at low levels, conferring resistance to 

\textit{TABLE 1. Antimicrobial susceptibility profiles of wild-type \textit{K. oxytoca} and \textit{K. oxytoca} OXY-2 hyperproducer strains evaluated in this study}

<table>
<thead>
<tr>
<th>Isolate</th>
<th>AMK</th>
<th>GEN</th>
<th>AMP</th>
<th>SAM</th>
<th>AMC</th>
<th>FEP</th>
<th>CRO</th>
<th>CAZ</th>
<th>CFX</th>
<th>CEX</th>
<th>CIP</th>
<th>MEZ</th>
<th>TZP</th>
<th>PIP</th>
<th>TIM</th>
<th>CTT</th>
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<td>&gt;64</td>
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* MIC values were determined by broth microdilution technique (3). AMK, amikacin; AMC, amoxicillin-clavulanic acid; AMP, ampicillin; FEP, cefepime; CRO, ceftriaxone; CAZ, ceftazidime; CFX, cefuroxime; CEX, cefoxithin; CIP, ciprofloxacin; GEN, gentamicin; IPM, imipenem; MER, meropenem; ATM, amoxicillin-clavulanic acid (AMC); TZP, piperacillin-tazobactam; PIP, piperacillin; TIM, ticarcillin-clavulanic acid; CTT, cefoxitin; SXT, trimethoprim-sulfamethoxazole.
We thank the personnel of ALERTA, LEMC, and CEMIC for their contributions during the performance of this study and especially Jussi-mara Monteiro for performing the PFGE technique.

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