First report of the bla<sub>OXA-58</sub> gene in a clinical isolate of 
Acinetobacter baumannii in Rio de Janeiro, Brazil

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Carbapenemase production is an important mechanism of carbapenem resistance among nonfermentative Gram-negative isolates. This study aimed to report the detection of bla<sub>OXA-58</sub> gene in multiresistant clinical isolates of Acinetobacter baumannii recovered from inpatients in a public hospital. Polymerase chain reaction tests were performed to detect the bla<sub>OXA-23-like</sub>, bla<sub>OXA-24-like</sub>, bla<sub>OXA-51-like</sub> and bla<sub>OXA-58-like</sub> genes. The bla<sub>OXA-58</sub> and bla<sub>OXA-23-like</sub> genes were detected in one and three isolates, respectively. Sequencing of the bla<sub>OXA-58-like</sub> amplicon revealed 100% identity with the A. baumannii bla<sub>OXA-58-like</sub> gene listed in the GenBank database. This is the first report of an OXA-58-producing A. baumannii isolate in Rio de Janeiro, Brazil.

Key words: Acinetobacter baumannii - oxacillins - OXA-58

Multidrug-resistant Acinetobacter baumannii is recognised as an important cause of nosocomial infections and a major problem confronting the intensive care unit due to its association with severe infections and the development of resistance to the major classes of antimicrobial agents (Bergogne-Bérézin & Towner 1996). According to the Meropenem Yearly Susceptibility Test Information Collection reports, A. baumannii was the fourth most prevalent pathogen isolated from hospitalised patients at 20 Brazilian centres and it presented high rates of resistance to all antimicrobial agents tested (Kiffer et al. 2005). Furthermore, several studies have shown the geographically widespread occurrence of carbapenem-resistant A. baumannii isolates over the last 10 years in Europe, North America and Latin America (Peleg et al. 2008).

Four OXA-type carbapenemases (Ambler class D) have been identified in A. baumannii: OXA-23-like (OXA-23, OXA-27 and OXA-49), OXA-24-like (OXA-24, OXA-25, OXA-26, OXA-40 and OXA-72), OXA-58-like and OXA-51-like. The identification of OXA-143 in carbapenem-resistant A. baumannii isolates in Brazilian hospitals was recently reported (Antonio et al. 2011). OXA-51-like constitutes a family of chromosomal enzymes typically present in A. baumannii. Outbreaks of OXA-23-producing A. baumannii have been reported worldwide, including in Brazil (Dalla-Costa et al. 2003, Naas et al. 2005, Zong et al. 2008, Carvalho et al. 2009, Kohlengberg et al. 2009). The occurrence of bla<sub>OXA-58</sub> in Acinetobacter spp is geographically widespread and consistently associated with resistance not only to carbapenems but also to many other antimicrobials, such as β-lactams, fluoroquinolones and aminoglycosides (Coelho et al. 2006, Peleg et al. 2008).

In the present study, we investigated the occurrence of genes associated with the production of carbapenem hydrolysing oxacillins among A. baumannii isolates recovered from inpatients at Hospital Estadual Azevedo Lima (HEAL), a 200-bed tertiary care centre located in Niterói, state of Rio de Janeiro, Brazil.

Twenty consecutive multidrug-resistant A. baumannii isolates recovered from inpatients at HEAL from October 2005-June 2006 were evaluated in the present study. Only one isolate for patient was included in the analysis. The isolates were identified by both conventional and semi-automated methods (Microscan, Dade Behring, West Sacramento, CA, USA). The disk diffusion method was performed to determine the antimicrobial susceptibility of the isolates according to the Clinical and Laboratory Standards Institute guidelines (CLSI 2010) using the following antimicrobial agents: amikacin, ampicillin/sulbactam, cefepime, cefazidime, ciprofloxacin, gentamicin, imipenem, meropenem, piperacillin/tazobactam, sulfamethoxazole/trimethoprim and tobramycin. Quality control testing was performed using Pseudomonas aeruginosa ATCC 27853 and Escherichia coli ATCC 25923. Genes encoding oxacillins classified as OXA-23-like, OXA-24-like, OXA-51-like and OXA-58-like were investigated by multiplex polymerase chain reaction (PCR) as de-
OXA-58-producing \textit{A. baumannii} in Brazil • Deuseli Quaresma de Figueiredo et al.

TABLE

Characteristics of four \textit{bla}_{OXA}\textsuperscript{+} carrying \textit{Acinetobacter baumannii} isolates detected in this study

<table>
<thead>
<tr>
<th>Strain</th>
<th>Date of isolation</th>
<th>Ward</th>
<th>Isolation site</th>
<th>Antimicrobial resistance profile</th>
<th>PCR products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ab554</td>
<td>May 11 2005</td>
<td>ICU</td>
<td>CVC</td>
<td>AMI, CAZ, CIP, FEP, GEN, IPM, MER, SXT, TOB, TZP</td>
<td>\textit{bla}<em>{OXA}\textsuperscript{+}/\textit{bla}</em>{OXA-58}</td>
</tr>
<tr>
<td>Ab680</td>
<td>August 15 2005</td>
<td>MU</td>
<td>TA</td>
<td>AMI, CAZ, CIP, FEP, GEN, IPM, MER, SXT, TOB, TZP</td>
<td>\textit{bla}<em>{OXA}\textsuperscript{+}/\textit{bla}</em>{OXA-23}</td>
</tr>
<tr>
<td>Ab822</td>
<td>May 18 2006</td>
<td>ICU</td>
<td>TA</td>
<td>AMI, CAZ, CIP, FEP, GEN, IPM, MER, SXT, TOB, TZP</td>
<td>\textit{bla}<em>{OXA}\textsuperscript{+}/\textit{bla}</em>{OXA-23}</td>
</tr>
<tr>
<td>Ab827</td>
<td>June 29 2006</td>
<td>MU</td>
<td>SS</td>
<td>CAZ, CIP, FEP, GEN, IPM, MER, SXT, TOB, TZP</td>
<td>\textit{bla}<em>{OXA}\textsuperscript{+}/\textit{bla}</em>{OXA-23}</td>
</tr>
</tbody>
</table>

AMI: amikacin; CAZ: ceftazidime; CIP: ciprofloxacin; CVC: central venous catheter; FEP: cefepime; GEN: gentamicin; ICU: intensive care unit; IPM: imipenem; MER: meropenem; MU: medical unit; PCR: polymerase chain reaction; SS: surgical site; SXT: trimethoprim/sulfamethoxazole; TA: tracheal aspirate; TOB: tobramycin; TZP: piperacillin/tazobactam.

ACKNOWLEDGEMENTS

To Dr Ana C Gales (Laboratório Alerta, Disciplina de Infectologia, Universidade Federal de São Paulo, São Paulo, Brazil), Dr Pierre Bogauts and Dr Caroline Bowing (CliniquesUniversitaires, UCL, Mont-Galline, Belgium), for providing OXA positive control strains.

REFERENCES


The worldwide dissemination of \textit{bla}_{OXA} genes in \textit{A. baumannii} is a growing concern, as these strains are resistant to almost all other antibiotics in addition to the carbapenems. This is the first report on the occurrence of the \textit{bla}_{OXA-23} and \textit{bla}_{OXA-58} genes in \textit{A. baumannii} recovered in the cities of Niterói and Rio de Janeiro, respectively. A recent study also reported the isolation of \textit{A. baumannii} carrying the \textit{bla}_{OXA-58} gene in São Paulo, another major Brazilian city (Antonio et al. 2011). The high clonal diversity of OXA-23-producing \textit{A. baumannii} indicates that control the dissemination of this pathogen may be difficult (Mugnier et al. 2010, Grosso et al. 2011). Further molecular and epidemiological studies are necessary to estimate the occurrence of these resistance determinants in different areas of a large country such as Brazil.

scribed previously (Woodford et al. 2006). PCR products were purified using the GTX PCR and band purification kit (GE Healthcare, Buckinghamshire, UK) according to the manufacturer’s instructions and were sequenced in an automated sequencer (MegaBACE 1000, GE Healthcare).

PCR analysis was performed with specific primers for all Ambler class D oxacillinases (OXA enzymes) and the \textit{bla}_{OXA-58} and \textit{bla}_{OXA-23} genes were detected in one and three isolates, respectively. PCR amplification products for acquired carbapenemase genes were not obtained from the other 16 isolates. All strains were positive for the \textit{bla}_{OXA-51} gene, an intrinsic enzyme-encoding gene characteristic of \textit{A. baumannii}, and no isolates presented the \textit{bla}_{OXA-24-like} gene.

Among the 20 \textit{A. baumannii} isolates, only those carrying the \textit{bla}_{OXA-58} and \textit{bla}_{OXA-23} genes were resistant to carbapenems, which is consistent with previous observations (Héritier et al. 2005). Of the three \textit{bla}_{OXA-23}\textsuperscript{+}-positive isolates, one was susceptible only to ampicillin/sulbactam and two were also susceptible to amikacin and tobramycin. The \textit{bla}_{OXA-58}\textsuperscript{+}-positive isolate (strain Ab554) was only susceptible to ampicillin/sulbactam (Table).

The 599 bp \textit{bla}_{OXA-58} amplicon obtained from isolate Ab554 was sequenced and analysed using the BLAST tool (www.ncbi.nlm.nih.gov/BLAST), showing 100% identity with the \textit{bla}_{OXA-58} gene sequence deposited in the GenBank database (accession HQ219687).

The worldwide dissemination of \textit{bla}_{OXA} genes in \textit{A. baumannii} is a growing concern, as these strains are resistant to almost all other antibiotics in addition to the carbapenems. This is the first report on the occurrence of the \textit{bla}_{OXA-23} and \textit{bla}_{OXA-58} genes in \textit{A. baumannii} recovered in the cities of Niterói and Rio de Janeiro, respectively. A recent study also reported the isolation of \textit{A. baumannii} carrying the \textit{bla}_{OXA-58} gene in São Paulo, another major Brazilian city (Antonio et al. 2011). The high clonal diversity of OXA-23-producing \textit{A. baumannii} indicates that control the dissemination of this pathogen may be difficult (Mugnier et al. 2010, Grosso et al. 2011). Further molecular and epidemiological studies are necessary to estimate the occurrence of these resistance determinants in different areas of a large country such as Brazil.


