Successful Eradication of a Monoclonal Strain of *Klebsiella pneumoniae* during a *K. pneumoniae* Carbapenemase-Producing *K. pneumoniae* Outbreak in a Surgical Intensive Care Unit in Miami, Florida

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We describe the investigation and control of a *Klebsiella pneumoniae* carbapenemase–producing *K. pneumoniae* outbreak in a 20-bed surgical intensive care unit during the period from January 1, 2009 through January 1, 2010. Nine patients were either colonized or infected with a monoclonal strain of *K. pneumoniae*. The implementation of a bundle of interventions on July 2009 successfully controlled the further horizontal spread of this organism.

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*Klebsiella pneumoniae* carbapenemases (KPCs) are coded by plasmid-mediated genes that confer resistance to all β-lactams. In addition, enteric bacteria that carry KPCs are most frequently resistant to other classes of antibiotics, such as fluoroquinolones and aminoglycosides. The most reliable treatment options for KPC-producing gram-negative bacilli are the polymyxins and, in some cases, tigecycline.

KPCs were discovered initially in the United States in 1996. Since then, an expansion of KPC-producing strains of bacteria has occurred worldwide. Mortality among patients infected with KPC-producing gram-negative bacilli is high (ie, approximately 40%). Because of the limited antibiotic options for treatment, prevention constitutes the main intervention to combat these organisms. We describe the investigation and successful control of an outbreak of KPC-producing *K. pneumoniae* due to a monoclonal strain in a surgical intensive care unit (SICU).

**METHODS**

This outbreak investigation was conducted in a 40-bed SICU at a 1,500-bed public teaching hospital in Miami, Florida. This SICU is physically divided into 2 units (SICU-A and SICU-B, which have 20 beds each). All consecutive patients with ertapenem-nonsusceptible *K. pneumoniae* during the period from January 1, 2009, to January 1, 2010, were identified by use of the clinical microbiology laboratory database and were evaluated by a healthcare worker from the infection control department. Data collected included patient demographic characteristics, dates of SICU admission, dates of culture results, and comorbidities.

Any *K. pneumoniae* isolate identified as ertapenem nonsusceptible by use of an antimicrobial susceptibility test (Vitek 2; bioMérieux) was tested by use of the modified Hodge test to confirm carbapenemase production. Susceptibility of isolates to polymyxin B was determined by use of broth microdilution, as described in the Clinical and Laboratory Standards Institute guidelines. Identification of *bla*KPC genes was done by polymerase chain reaction (PCR) using the following primers: KPCF: 5′-TGT CAC TGT ATC GCC GTG TGC TAG-3′ and KPCR: 5′-TTA CTT CCC GTT GAC GCC CAA TCC-3′. PCR conditions were as follows: 3 minutes at 94°C and 30 cycles of 1 minute at 94°C, 1 minute at 52°C, and 1 minute at 72°C, followed by an elongation step for 10 minutes at 72°C which produced a band of 880 bp encompassing the entire KPC coding region. PCR was performed by use of HiFi Platinum Taq DNA Polymerase (Invitrogen). Sequencing was done by Agen- court Bioscience.

Pulsed-field gel electrophoresis (PFGE) was performed by use of the CHEF-DR II system with the CHEF Mammalian DNA plug kit and the GenePath Group 6 reagent kit, according to the instruction manual, with modifications specific for *K. pneumoniae* (BioRad). DNA was electrophoresed for 22 hours at 14°C in a 1% agarose gel at a field strength of 6 V/cm and with a linear gradient pulse time of 2.2–54.2 seconds. The pulsed-field gels were interpreted according to the criteria of Tenover et al.

On the basis of the distribution of cases of KPC-producing *K. pneumoniae* in the hospital, an infection control bundle was implemented in SICU-B starting in mid-July 2009. This bundle consisted of the following elements.

Beginning on July 11, daily baths were performed with 2% chlorhexidine impregnated wipes (Sage) on all SICU-B patients. Healthcare workers in SICU-B were educated on the use of and rationale for these wipes. Soap that was previously used for patients’ baths was removed from the unit’s shelves. Episodes of stool incontinence were cleaned with cotton cloths and water, as needed.

Point-prevalence surveillance was performed on August 5 and 18, 2009. Rectal samples were obtained from patients by use of double rayon swabs in liquid Stuart transport medium (BBL CultureSwab; BD Diagnostics). All patients present in SICU-B (except those patients already confirmed as having KPC-producing *K. pneumoniae*) had their rectal samples cul-
still hospitalized as of February 2010.

disk of imipenem and reincubated overnight at 37°C. Growth was subcultured on MacConkey agar with a 10-μg disk of imipenem and reincubated overnight at 37°C. Isolates were tested by use of both the modified disk (final concentration of imipenem, 2 μg/mL). Broths were placed in 5 mL of tryptic soy broth with a 10-μg imipenem disk (final concentration of imipenem, 2 μg/mL). Broths were incubated overnight at 37°C. Any tube with evidence of growth was subcultured on MacConkey agar with a 10-μg disk of imipenem and reincubated overnight at 37°C. K. pneumoniae isolates were tested by use of both the modified Hodge test and PCR testing, as described above.

Patients identified as colonized or infected with KPC-producing K. pneumoniae were placed in private rooms whenever feasible or cohorted in an open, 4-patient pod. Respiratory therapists, nursing staff, and nursing aids were also cohorted during their shifts and on a rotating basis, to care exclusively for patients known to harbor KPC-producing K. pneumoniae. Additional educational campaigns (in services) were provided to all SICU-B personnel regarding KPC-producing K. pneumoniae. These campaigns were implemented by the infection control department and emphasized the relevance of contact precautions (ie, the use of gowns and/or gloves) and cohorting.

**RESULTS**

Ten patients colonized or infected with KPC-producing K. pneumoniae were identified at our hospital during the 12-month study. One patient was bacteremic and had KPC-producing K. pneumoniae on the day he or she was transferred from a Venezuelan hospital in November 2009. This patient was not analyzed.

The 9 remaining patients were located in SICU-B, which is a 20-bed unit with 5 private rooms and an open, 4-patient pod. The bundle of interventions was implemented consecutively during the last 3 weeks of July 2009. The bundle was fully instituted by the end of July, and only 2 patients with KPC-producing K. pneumoniae were identified thereafter (Figure 1).

Most patients with KPC-producing K. pneumoniae were elderly (median age, 60 years) and male (7 [78%] of 9 patients), and they had a high acuity of illness (Acute Physiology and Chronic Health Evaluation II score [± standard deviation], 18 ± 6.6) and multiple medical comorbidities (mean Charlson comorbidity score [± standard deviation], 5.3 ± 1.8). Of the 9 patients, 5 (56%) had received a solid organ transplant. The mean number of days to a culture result positive for KPC-producing K. pneumoniae was 59.5 days (range, 0–186 days). KPC-producing K. pneumoniae was isolated in urine (11 isolates), bronchoalveolar lavage fluid (5 isolates), peritoneal fluid (2 isolates), and blood samples (1 isolate). The mean number of culture results positive for KPC-producing K. pneumoniae per patient was 6.5 (range, 1–14). Six patients (67%)—including 3 organ transplant recipients—died; 4 of these 6 patients died of sepsis.
Clinical isolates were found to be monoclonal KPC-3 producers. Eight KPC-producing *K. pneumoniae* isolates (88%) were susceptible to imipenem (minimum inhibitory concentration [MIC] of 1 μg/mL or less), 4 isolates (44%) were susceptible to meropenem (MIC of 1 μg/mL or less, confirmed by use of a broth microdilution method), all isolates were either resistant or nonsusceptible to piperacillin-tazobactam, and all were resistant to ciprofloxacin. Only 1 isolate was found to have a high MIC for polymyxin B (MIC of 16 μg/mL).

Of the 15 environmental surfaces for which swab samples were obtained for culture, 10 (67%) grew KPC-producing *K. pneumoniae* on culture. In a total of 3 rooms of patients colonized with KPC-producing *K. pneumoniae*, environmental surface samples were obtained for culture, and in all 3 rooms, it was found that the samples obtained from the bed rails, mattresses, corrugated ventilator tubing, intravenous poles, vital-sign monitors, and television monitors all grew KPC-producing *K. pneumoniae* on culture. A swab sample positive for KPC-producing *K. pneumoniae* on culture was also obtained from the keyboard of a “computer on wheels” outside 1 of the 3 rooms. The PFGE patterns of these environmental isolates were identical to those of the clinical isolates.

On July 10, UV light surveillance data showed that the surfaces of the mechanical ventilators and bed rails in 3 rooms occupied by patients colonized with KPC-producing *K. pneumoniae* were not being cleaned. Furthermore, we discovered that neither environmental services’ personnel nor nursing staff were cleaning bed rails on a daily basis in any of the rooms. Subsequently, a multidisciplinary team was convened to assign cleaning responsibilities for each high-touch surface in the patients’ rooms.

During the first point-prevalence surveillance period (ie, August 5), 19 patients were screened; rectal swab samples were obtained for culture from all 19 patients, and endotracheal secretion samples were obtained for culture from 9 patients. Of the 19 patients screened, 2 (11%) were found to be asymptomatic carriers of the outbreak strain; they both had stool and respiratory secretion samples that were positive for the monoclonal strain of *K. pneumoniae*. During the second point-prevalence surveillance period (ie, August 18), 12 patients were screened; rectal swab samples were obtained for culture from all 12 patients. No strains of KPC-producing bacteria were detected. On the basis of environmental culture results, all patients colonized with KPC-producing *K. pneumoniae* had their corrugated ventilator tubing exchanged every 48 hours during the period from August 1, 2009, until the last patient receiving mechanical ventilation was either discharged or extubated.

**Discussion**

We describe the eradication of a monoclonal strain of *K. pneumoniae* during a KPC-producing *K. pneumoniae* outbreak in an ICU at a large teaching hospital. Prior to this outbreak, the last KPC-producing *K. pneumoniae* isolate identified as having been recovered from this unit occurred in November 15, 2007. A total of 9 patients were identified, and 6 of them died. During the outbreak investigation, we found both environmental samples (ie, from rooms of colonized patients) and clinical samples (ie, from colonized or infected patients) that were positive for the monoclonal strain of *K. pneumoniae* on culture. A bundle of interventions that included chlorhexidine baths, point-prevalence surveillance, environmental culture, cohorting of colonized patients and healthcare personnel, increased environmental cleaning, and staff education was implemented in mid-July 2009. Patterns of antibiotic use were not modified during the intervention months. Shortly after the implementation of this bundle of interventions, and at least while this manuscript was being written (February 2010), no new cases of KPC-producing *K. pneumoniae* were observed.

Because of the clonality and geographic clustering of the KPC-producing *K. pneumoniae* isolates in the hospital, the horizontal transmission of the outbreak strain most likely occurred in SICU-B. Positive environmental culture results suggest that the environment might have played a role in the outbreak; however, we do not have additional data to support this theory.

A few studies describe the management of outbreaks caused by KPC-producing gram-negative bacilli. All of them describe a combination of different interventions to control KPC-producing *K. pneumoniae* outbreaks.

Our study has various limitations, starting with the small number of patients. However, we strongly believe that, to be successful at eradicating KPC-producing *K. pneumoniae* from a hospital setting, interventions cannot wait until a larger number of patients become colonized or infected. Another limitation was the relatively short duration of follow-up. Also, we were unable to determine the mechanism of horizontal transmission of this *K. pneumoniae* strain, although we presume that this mechanism was related to violations in the use of contact precautions. Compliance with hand hygiene and with the use of gowns and gloves was not systematically monitored before or after the intervention started. Moreover, we will never know whether this outbreak would have waned without the implementation of any interventions; 2 studies of outbreaks of carbapenem-resistant *K. pneumoniae* (one in Israel and one in New York) suggest that that would have been an unlikely scenario.

KPC-producing organisms have proliferated rapidly worldwide, and regrettably there are limited treatment options available for those infected with these types of organisms. Thus, the medical community should concentrate their efforts on the prevention of further spread of these organisms within hospital settings. We believe that our experience will help guide clinicians in controlling future outbreaks of KPC-producing bacteria. Per a recent position paper by the Society
of Healthcare Epidemiology of America, additional studies are urgently needed in this rapidly changing field.

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