An effective intervention to limit the spread of an epidemic carbapenem-resistant *Klebsiella pneumoniae* strain in an acute care setting: From theory to practice

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Background: The highly transmissible and virulent carbapenem-resistant *Klebsiella pneumoniae* (CRKP) KPC-3 strain has been spreading in our medical center and in other centers in Israel since 2006. An intervention that aimed to diminish its prevalence was constructed and applied in our institute.
Methods: We analyzed the efficacy of the intervention during the years 2006-2010 using quasi-experimental methodology. The intervention included guidelines for patient isolation, cohorting, and environment cleaning; education of staff; and a computerized notification system that flags CRKP carriers and provides instructions. The efficacy of the program was evaluated through 3 quantifiable parameters: incidence of CRKP isolates from clinical samples, rate of cross-infections, and rate of screening for CRKP carriage in patients at risk identified by rectal samples.
Results: The incidence of CRKP decreased by 16-fold ($P < .001$), and this decrease was sustained for 30 months. The rate of cross-infection decreased from 6% during 2007-2008 to 2.7% in 2009-2010 ($P < .05$). This period saw an increased rate of active surveillance for carriers, from 20% to 89%.
Conclusions: A comprehensive infection control program can contain an outbreak of the CRKP KPC-3 strain in acute care hospitals during a nationwide outbreak of this strain.
Key Words: Carbapenem-resistant Enterobacteriaceae; cohorting; computerized system; containment; infection control; cross infection; quasi-experimental study.

A carbapenem-resistant *Klebsiella pneumoniae* (CRKP) strain was first described in 2001.[1] Reports of sporadic isolations and outbreaks in various countries over the last decade indicate that CRKP is spreading worldwide.[2-4] Infections due to CRKP have been identified as an independent risk factor for mortality.[5-7] During the second half of 2006, ~500 new cases were identified in Israel.[8] Shortly thereafter, CRKP became a nationwide epidemic[8] due to cross-transmission of a clonal KPC-3 strain among patients in hospitals and long-term care facilities (LTCFs).[9] The virulence and remarkable transmissibility of the KPC-3 strain, combined with limited therapeutic options and the inability to eradicate it, have underscored the need to intensify existing local infection control measures while seeking innovative infection control actions.

In 2007, the Israeli Ministry of Health issued general guidelines for containing CRKP,[10] and subsequently the Centers for Disease Control and Prevention (CDC) published guidelines for containing carbapenem-resistant Enterobacteriaceae (CRE).[11] In parallel with these guidelines, we developed a comprehensive infection control intervention at the Kaplan Medical Center (KMC), an acute care hospital. The program included cohorting and isolating affected carriers as well as enhancing team compliance through education and enforcement. These measures were complemented by an automated system using the computerized patient chart in which new cases were reported and immediate instructions were issued for isolation, cohorting, and active screening. Here we describe this intervention in detail and provide evidence of its success: a 16-fold

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decrease in the incidence of CRKP that was sustained for 30 months.

METHODS

Setting

KMC is a 535-bed secondary regional hospital with a thoracic surgery service and a 230-bed rehabilitation and LTCF branch, affiliated with the Hebrew University School of Medicine. The hospital has an average of 55,000 admissions per year, with 177,000 hospitalization-days and a yearly occupancy of ~85%. Most patients are in 4-bed rooms, and typically the same nursing staff treats roommates. KMC medical charts are completely computerized.

Identification of CRKP and susceptibility tests

K pneumoniae isolates were identified using the VITEK 2 automated microbiology system (bioMerieux, Marcy l'Etoile, France). The laboratory used updated identification methods for screening and identifying CRKP, namely CHROMagar KPC (Hy Laboratories, Rehovot, Israel)[12] and the modified Hodge test, according to Clinical and Laboratory Standards Institute guidelines.[13] Antibiotic susceptibility profiling was done automatically using the VITEK 2 system, and the minimal inhibitory concentration (MIC) for carbapenems (ertapenem, imipenem, and meropenem), colistin (polymyxin E), and tigecyclin was determined by epsilometer tests (Etests).

CRKP characterization

Eight clinical isolates from KMC and 6 isolates from the LTCF obtained at the outset of the 2006 outbreak were studied as a part of a nationwide characterization of CRKP as described by Navon-Venezia et al.[9] The presence of bla_{KPC} and bla_{TEM} was verified using polymerase chain reaction (PCR) followed by sequence analysis to identify the specific KPC gene.[14] The genetic relatedness of CRKP strains was determined by pulsed-field gel electrophoresis (PFGE).[14] Molecular studies characterized the KPC-3–encoding plasmid.[14] During 2007-2010, another 12 isolates were tested by PCR for the KPC gene; 3 of these also were tested for clonality by PFGE.

Definitions

A clinical case of CRKP was defined as CRKP isolated from blood culture or from a sample of pleural or peritoneal fluid, urine, respiratory tract, catheter tip, wound culture, or wound drain. A CRKP carrier was defined as a patient found to have CRKP solely in a rectal culture (unlike clinical cases of CRKP). Cross-infection was defined as a patient exhibiting positive rectal culture after a roommate's identification as a new clinical case or carrier. The rationale underlying this definition was that the same medical staff cared for the roommates of a newly identified CRKP case/carrier, and the rate of CRKP carriage in random patients was presumed to be very low.

Study design and time definition

The study was quasi-experimental. Surveillance was continued for 54 months, with a preintervention period from January 2006 through January 2007 and an intervention period from February 2007 through June 2010. Starting in June 2007, every roommate of a newly diagnosed CRKP case or carrier and all patients admitted to the intensive care unit were screened for CRKP using rectal swabs. In addition, starting in August 2008, screening of patients at high risk for CRKP carriage as defined previously[7] admitted to departments that admit $\geq$5% of their patients from LTCFs and nursing homes (eg, internal medicine, orthopedic, geriatrics) was instituted. Only the first positive culture from a patient (clinical case or carrier) was included in the study.

Performance evaluation

The efficacy of the intervention was assessed using 3 variables:

1. The incidence of clinical cases. Every new clinical case was reported to the infection control unit and recorded. The incidence rate was calculated periodically.
2. The rate of cross-infection, which is the proportion of CRKP-positive patients identified by rectal culture after identification of a new CRKP case (clinical/rectal colonization) out of all of the exposed patients who were recorded and tested.
3. The rate of screening for CRKP carriage in admitted patients with risk factors for CRKP carriage. Compliance with this type of active surveillance was assessed by determining the proportion of patients actually screened by hospital staff out of all the patients that should have been screened.

Intervention

The multidisciplinary intervention involved 3 key elements: (1) guidelines for cohorting, cleaning, and screening; (2) education and training; and (3) automatic instructions and CRKP alerts.

Guidelines for cohorting, cleaning, and screening. Clinical cases as well as carriers of CRKP were cohorted in separated locations. Identification of any new clinical case or carrier of CRKP mandated a survey for possible carriers as a result of cross-infection among roommates. The cohorted carriers were treated exclusively by dedicated nursing personnel. Strict contact precautions were implemented by the dedicated nursing