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Major article

Controlling outbreak of vancomycin-resistant *Enterococcus faecium* among infants caused by an endemic strain in adult inpatients

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Background: Vancomycin-resistant *Enterococcus faecium* (VREfm) is commonly associated with hospital outbreaks and has been found to be associated with increased morbidity, mortality, length of stay, and health care costs.

Methods: We sought to investigate and control an outbreak of VREfm in the neonatal intensive care unit (NICU) of a public academic hospital with a level III NICU. The index case was an infant in the NICU incidentally identified with urinary colonization with VREfm. Aggressive control measures were initiated promptly. Investigation included active surveillance cultures in infants, parents of colonized infants, and birth mothers of newborn admitted to NICU; molecular strain typing of available isolates of VREfm including adult inpatients; and medical record review.

Results: After identification of index case, 13 additional infants were identified with VREfm colonization. Age at culture was 6 to 87 days; birth weight was 1,070 to 2,834 g. VREfm isolated from majority of infants (12/14 [85.7%]), the birth mother of a pair of colonized twins, and a pulse oximeter device used in adult inpatients belonged to a single strain. Outbreak control measures were successful in the NICU. The outbreak-causing strain was found to be endemic among adult inpatients. Adult patients with the outbreak-causing strain of VREfm were more likely to have received previous therapy with meropenem (Mann-Whitney 2-tailed *P* value = .038). VRE colonization was identified in 0.3% (1/310) of birth mothers with newborn admitted to NICU.

Conclusion: An endemic strain of VREfm among adult inpatients was responsible for a subsequently controlled outbreak in the NICU.

Vancomycin-resistant *Enterococcus faecium* (VREfm) is commonly associated with hospital outbreaks. In adults, colonization or infection with VREfm has been found to be associated with increased morbidity, mortality, length of stay, and health care costs.[1-6] Treatment options are limited. Prompt outbreak recognition and timely implementation of infection control measures to avoid patient adverse effects via the infection itself or the need of antimicrobial therapy is therefore important. In this article, we describe the investigation and control efforts to contain an outbreak of VREfm in a neonatal intensive care unit (NICU) and the consequent implications for hospital-wide VREfm control.

METHODS

Setting

The setting was Parkland Memorial Hospital, a 672-bed, county tax-supported, tertiary care academic referral center that provides a wide range of services, including level I trauma, burn, transplantation, and high-risk obstetrics. Parkland Health and Hospital System provides health care to over 20% of the population of the Dallas metroplex area including a large proportion of indigent individuals. It is the primary teaching facility for the University of Texas Southwestern Medical Center in Dallas, Texas. The hospital

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Conflicts of interest: None to report.

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Table 1
Comparison of clinical characteristics of adults with outbreak-causing strain of VRE with those of adults with non-outbreak strain of VRE and vancomycin-susceptible *Enterococcus faecium*

	Outbreak strain VREfm (cases n = 20)		Non-outbreak strain VREfm (first control group, n = 20)		OR	95% Confidence interval	*P* value	Vancomycin-susceptible *Enterococcus faecium* (second control group, n = 20)		OR	95% Confidence interval	*P* value
	n or median	% or range	n or median	% or range				n or median	% or range			
Age at date of culture	48	(14-84)	51	(22-86)			.27	48	(14-90)			1.00
Female sex	10	50	12	60	1.50	0.42-5.25	.75	10	50			1.00
Inpatient	20	100	20	100			1.00	12	60			.003*
Body mass index	29	(18-63)	27	(16-55)			.11	26	(19-63)			.013*
Days of hospital stay within previous 1 year	19	(1-79)	18	(3-80)			.81	11	(0-80)			.002*
Days of ICU stay within previous 1 year	1	(0-52)	3	(0-24)			.64	0	(0-52)			.005*
Number of Surgeries within previous 1 year	11	55	14	70	1.91	0.52-7	.51	4	20	0.21	0.05-0.8	.048*
Ventilator care within 30 days of culture	5	25	8	40	2.00	0.52-7.72	.50	0	0			.047*
Selected antimicrobial days within 30 days of culture												
Vancomycin	4	(0-20)	1	(0-17)			.16	0	(0-20)			.00*
Any cephalosporin	0	(0-12)	0	(0-17)			.46	0	(0-3)			.004*
Meropenem†	0	(0-19)	0	0			.038*	0	(0-19)			.038*
Clindamycin or metronidazole	0	(0-25)	0	(0-15)			.44	0	0			.048*
Any fluoroquinolone	0	(0-13)	0	(0-8)			.12	0	(0-10)			.019*
Outcomes												
Home	12	60	13	65	1.24	0.34-4.46	1.00	19	95	12.67	1.4-114.4	.019*
Long-term acute care or nursing facility	5	25	4	20	0.75	0.17-3.33	1.00	0				.047*

*P value $\leq .05$.
†Only carbapenem used in the study patients.

has a level III NICU operating at 65 beds with surge capacity to 90 beds, and 1,400 admissions annually.

Outbreak investigation

In May 2010, a neonate in the NICU was incidentally identified with urinary colonization caused by VREfm during evaluation for sepsis. There was no active surveillance program for VREfm in the NICU or the obstetric population during this time. Because the previous case of VRE occurred in the NICU over 5 years prior to this occurrence, outbreak investigation and control efforts were initiated. Weekly active surveillance cultures by rectal swabs to identify rectal colonization with VRE were begun in the NICU to identify the extent of transmission initially and to monitor ongoing transmission. Preliminary control measures were implemented. Epidemic curve was drawn to trend the weekly incidence of VRE in the NICU. Medical record review was performed to identify the clinical characteristics of infants identified with VREfm. Antimicrobial use patterns were examined in the NICU during the preceding 6 months. To evaluate the source for the outbreak, parents of the colonized infants were screened for presence of VREfm colonization. To identify clonal relatedness of isolates, strain typing was performed with repetitive element polymerase chain reaction (rep-PCR).

When clonal transmission was identified among the infants, and the outbreak strain was identified in a birth mother of a pair of colonized twins, further strain typing of available VREfm isolates from adult hospital inpatients was performed. These isolates had been obtained for clinical indications during routine patient care. Environmental cultures were performed in the adult hospital wards. Environmental cultures were not performed in the NICU prior to thorough environmental cleaning because cleaning was done immediately after identification of the outbreak. However, confirmatory negative environmental cultures were obtained after thorough cleaning. Because the outbreak-causing strain of VREfm in the NICU was found to be endemic in the adult non-obstetric hospital wards, a case-control study was performed to identify clinical factors associated with presence of outbreak-causing strain of VREfm among the adult hospital inpatients admitted between February and September 2010. There was no active surveillance program for VRE among adult inpatients at the time of occurrence of this outbreak. The clinical characteristics of adult inpatients with outbreak-causing strain of VREfm (n = 20; cases) were compared with those of an equal number of adult inpatients with any different strain of VREfm (n = 20; control group 1) and adult patients with vancomycin-susceptible *Enterococcus faecium* (inpatient or outpatient; n = 20; control group 2), matched by date of identification of VREfm or vancomycin-susceptible *Enterococcus faecium* during the same month as the case patient. These isolates had been obtained for clinical indications during routine patient care. Clinical characteristics and outcomes were identified through review of medical records. The candidate variables included were based on literature review. The statistically significant variables are listed in Table 1. Other tested variables with a P value $\geq .05$ in univariate analysis included Charlson comorbidity index, days of tunneled or non-tunneled catheter use within 30 days of culture, any penicillin or antifungal antimicrobial used within 30 days of culture, methicillin-resistant *Staphylococcus aureus* or *Clostridium difficile* positivity, and all-cause mortality. Meropenem is the carbapenem antimicrobial mostly used at the study institution and the only carbapenem found to be used in the study patients.

To assess prevalence of VREfm colonization among birth mothers whose newborns were admitted to the NICU, active