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Re-institution of Reflex Testing of Stool Samples for Vancomycin-Resistant Enterococci (VRE) Resulted in Decreased Incidence of Hospital-Associated VRE

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Narrative Abstract

Re-institution of reflex testing of stool submitted for *Clostridium difficile* testing for vancomycin-resistant enterococci (VRE) reduced the incidence of healthcare-associated VRE bacteremia and bacteriuria compared to when testing was not in place (1.9 versus 3.3 cases per 10,000 patient days when testing was not in use).

Keywords

Vancomycin resistance; *Clostridium difficile*; enterococci; Patient isolation; Feces; Microbiology; Bacteremia; Bacteriuria

Introduction

Vancomycin-resistant enterococci (VRE) infections result in increased hospital costs and length of stay (1). Previously, we described a hospital-wide “reflex” testing program for detecting VRE intestinal colonization as an intervention to limit nosocomial transmission. Inpatients that had diarrheal stools submitted to the clinical microbiology laboratory for *Clostridium difficile (C. difficile*) toxin testing also had screening cultures for VRE (2). In July 2010, this program was discontinued and in the subsequent 18 months, the monthly incidence of healthcare-associated VRE increased by 71%.

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Based on these findings the VRE reflex testing program was re-instituted in January 2012. We examined the effect of re-institution of the VRE reflex testing program on healthcare-associated VRE incidence.

Methods

Barnes-Jewish Hospital is a 1,250-bed academic tertiary care hospital in Saint Louis, Missouri. We examined the healthcare-associated VRE rate between January 2009 and December 2015. Reflex testing for VRE was discontinued in July 2010 and re-instituted in January 2012. Clinicians were notified of these changes to VRE reflex testing. Throughout the study period, clinicians could order stool or peri-rectal cultures for VRE testing at their discretion. Hospital policy during the study was to place VRE colonized or infected patients in contact precautions in a private room. During the reflex screening period 1 (January 2009 to July 2010), stool specimens were plated out on BD Enterococcosel Agar (Becton Dickinson, Sparks, Maryland). In the screening period 2 (January 2012 to December 2015), chromID VRE (bioMerieux, Durham, NC) was used. There was no difference in the screening cultures performed that were positive for VRE in either screening periods [25.5% (2457/9637) in period 1 versus 25.2% (6289/24920) in period 2; $p = 0.62$].

All hospitalized patients with a positive urine or blood culture for VRE were identified. A healthcare-associated VRE case was defined as the first positive specimen per patient, where VRE was detected in blood or urine ≥ 3 calendar days after admission. A VRE case was considered present on admission if VRE was detected in blood or urine < 3 calendar days after admission (3). In the original study, we defined healthcare-associated VRE as initial culture within 48 hours after admission. The VRE incidence was expressed as cases per 10,000 patient-days.

The effect of reflex testing on the incidence of healthcare-associated VRE was evaluated using regression models with autoregressive integrated moving average (ARIMA) errors. In addition to reflex testing, VRE prevalence on admission, central line utilization, urinary catheter utilization, and overall temporal trend were considered in the model to evaluate the effects of these factors on healthcare-associated VRE rate during the study period. The Washington University Human Research Protection Office approved this study.

Results

There were 99 cases [blood =36 (36.3%), urine =63 (66.6%)] of healthcare-associated VRE (2.3/10,000 patient-days) in the initial reflex testing period, 166 cases [blood=63 (38.0%), urine=103 (62.0%)] when reflex testing was discontinued (3.7/10,000 patient-days), and 218 cases [blood=57 (26.1%), urine=161 (73.9%)] after reflex testing was re-instituted (1.8/10,000 patient-days) (Figure). Accounting for the overall temporal trend, healthcare-associated VRE decreased at a rate of 36.4% (−36.4, 95% CI: −50.9, −17.7) per month during the entire study period. The average healthcare-associated VRE rate was 1.9/10,000 patient-days during the reflex testing periods, versus 3.7/10,000 patient-days during the non-testing period. When adjusted for VRE prevalence on admission and overall temporal trend,

reflex testing was associated with 32.0% (−32.0; 95% CI: −48.2, −10.8) reduction in healthcare-associated VRE incidence compared to the non-reflex testing period.

Conclusion

In this follow-up study, we noted that hospital-wide re-institution of a VRE reflex screening program led to a decrease in hospital-associated VRE incidence to a baseline rate similar to pre-discontinuation period, which further suggested a causal relationship between the program and a reduction in hospital-associated VRE transmission (4). Most hospitals, often due to the lack of routine active surveillance, do not identify a large proportion of colonized patients who are potential sources for ongoing hospital transmission (5, 6). Some studies have demonstrated the benefit of active surveillance cultures to control VRE transmission in hospitals; however, these were generally done during an outbreak in which multiple interventions were introduced simultaneously (7, 8). In our previous study, we found that discontinuation of reflex VRE testing of stool submitted for testing for *C. difficile* at our hospital resulted in a 71% increase in the endemic healthcare-associated VRE rate (Figure). This long-term, follow-up analysis suggested that when reflex VRE testing was re-implemented, healthcare-associated VRE rates returned to our pre-discontinuation baseline.

Limitations of our study included data from a single care center and lack of information on patient-level characteristics. Other concern may be due to change in the screening method of stool specimens. However, the percent of positive screening tests did not change significantly. Strengths of the study include repeated treatment design (9) and use of regression models with ARIMA errors to appropriately account for correlated observations over time and to adjust for the overall temporal trend and important confounders such as VRE prevalence on admission. Furthermore, no other specific infection prevention measures were implemented over the study timeframe, and laboratory methods for identifying VRE from urine and blood cultures did not change. Also there were no outbreaks of *C. difficile* during this period.

In conclusion, we found that the use of VRE reflex testing of stool submitted to *C. difficile* testing was effective in reducing the incidence of hospital-associated VRE infections when combined with contact precautions program. This should be considered as a valid strategy to reduce VRE transmission in hospital settings.

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Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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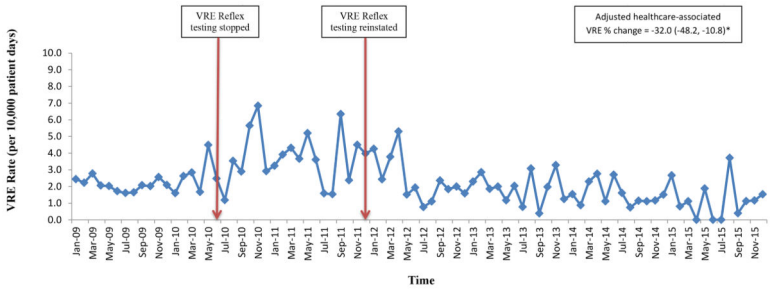

Figure.

Monthly incidence of healthcare-associated vancomycin resistant enterococci (VRE) infections, January 2009 – December 2015

*Rate adjusting for overall temporal trend and VRE prevalence on admission by Autoregressive integrated moving average.