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Review

Controlling the spread of vancomycin-resistant enterococci. Is active screening worthwhile?

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SUMMARY

Vancomycin-resistant enterococci (VRE) are significant causes of healthcare-acquired infections. Active screening, i.e. the use of rectal swabs or faeces to detect carriage in at-risk patients, has been described as contributing to prevention by identifying previously unrecognized cases. The aim of this review was to determine the impact of screening for VRE on prevention and control, its cost-effectiveness and recent approaches to laboratory detection. A review of published studies in English from 2000 was undertaken. Whereas various guidelines were accessed and reviewed, the emphasis was on original reports and studies. It was determined that the patient groups who may need screening are those admitted to critical care units, haematology/oncology and transplant wards, patients on chronic dialysis and patients admitted to acute hospitals from long-stay units. Active screening is associated with reduced VRE colonization and infection and cost savings in some studies, even if these fall short of randomized trials. Selective media increase sensitivity and reduce the time to detection but the role of molecular methods remains to be determined. In conclusion, active screening contributes to VRE prevention probably by heightening awareness of control measures, including isolation. However, further studies are required to: better define high-risk groups that warrant screening; quantify the clinical and economic benefit; and determine the optimal laboratory methods in a range of different patient populations.

Introduction

Enterococci are part of the normal bacterial flora of the gastrointestinal tract of humans. The most important species are *Enterococcus faecalis* and *Enterococcus faecium*, which may cause significant infections including bloodstream infection (BSI).[1] Enterococci are considered intrinsically resistant to some antibiotics such as the cephalosporins; consequently glycopeptides have been the mainstay of treatment as there are few other options for treatment. Vancomycin-resistant enterococci (VRE) were first isolated in the late 1980s and they have spread rapidly throughout the USA, Europe, and beyond.[2,3]

Vancomycin-resistant enterococci are important causes of healthcare-associated infection (HCAI), often affect the most vulnerable patient groups, and cause considerable mortality with additional healthcare costs. Recent data from the National Healthcare Safety Network in the USA indicate that enterococci were the second most frequent cause of HCAIs after *Staphylococcus aureus* and that 89% of *E. faecium* isolates causing central line-associated BSI were vancomycin resistant.[4] In a recent European survey of >230,000 patients in nearly 1000 acute hospitals, enterococci were the third most common cause, of which 10% were VRE.[5]

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Patients with BSI due to VRE are more likely to die than are those with BSI caused by vancomycin-susceptible enterococci (VSE), vancomycin resistance is an independent predictor of mortality, the median duration of BSI is longer for VRE compared with VSE, and VRE acquisition is associated with a longer duration of hospital stay.[6–8] In Canada the mean total costs and length of stay (LOS) for patients with VRE have been calculated to be significantly higher compared to those for VRE-negative patients, i.e. C$46,924 and 34 days versus C$13,069 and 10.9 days, respectively.[9] The US Centers for Disease Control and Prevention have recently highlighted VRE as resistant bacteria of serious concern that require prompt and sustained action.[10] Whereas there has been a much-needed emphasis in recent years on the importance of *Clostridium difficile* infection and the threat posed by multidrug-resistant Gram-negative bacilli, such as carbapenem-resistant Enterobacteriaceae, VRE remain important. Hence it is opportune to review the indications for, and value of, screening for VRE. The purpose of screening is to identify carriers during outbreaks to assist in outbreak management, and in non-outbreak settings to prevent onward transmission, especially to vulnerable patient groups.

Methods

The scientific literature on the prevention and control of VRE published in English since 2000 until June 2014 was reviewed with searches conducted in PubMed, EMBASE, and CINAHL to access studies and other reports on VRE screening and the identification of risk factors that would inform screening strategies. Search terms used in addition to VRE included glycopeptide-resistant enterococci, antibiotic-resistant enterococci, including *E. faecalis* and *E. faecium*, epidemiology, clinical impact, risk factors, screening and surveillance, laboratory methods and diagnosis, individually as well as in combination. General terms such as infection prevention and control were also used. Emphasis was placed on sourcing and reviewing original papers describing controlled clinical trials or quasi-experimental studies involving screening, to prevent and control spread, and methods for laboratory detection. The reference list of papers obtained from the literature search was also reviewed to determine whether there were other relevant studies that should be assessed and included, but which were not detected in the original literature search. However, many reports describe multiple interventions during outbreaks and therefore it can be difficult to quantify or estimate the impact of screening compared with other measures, such as improved environmental hygiene and better antimicrobial stewardship.

Risk factors for VRE

Strategies to prevent and control VRE have been reviewed in the recent literature and in several guidelines and studies.[11–15] These recommend a multi-pronged approach that includes screening, improved professional practice such as hand hygiene, patient isolation, antibiotic stewardship, and enhanced environmental hygiene. Screening strategies should be devised to maximize the detection of carriers and should be informed by a knowledge of risk factors for VRE.

Intrinsic and extrinsic patient factors

Intrinsic risk factors associated with the patient include underlying illnesses, whereas extrinsic factors include exposure to a VRE-positive environment. However, many of these risk factors have been determined in studies that have varied considerably in size, population studied, and design. Nonetheless, some important and clinically relevant factors that predispose to VRE have been clearly recognized (Table I). As with other multidrug-resistant bacteria such as meticillin-resistant *Staphylococcus aureus* (MRSA), immunocompromised patients and those with significant underlying conditions are at greatest risk. A point prevalence survey of VRE, which detected vancomycin-resistant *E. faecium* in 32% of stool specimens, found that previous hospitalization, chronic renal failure, and

Table I
Risk factors for the acquisition of vancomycin-resistant enterococci

Risk factor	Comment	Reference
Intrinsic		
Immunosuppression	Includes haematology/oncology conditions, solid organ transplantation, and neutropenia	18,19
Renal dialysis	May relate to underlying renal disease or regular healthcare contact	16
Recent/current antibiotic use	Third-generation cephalosporin, fluoroquinolones and β-lactam/β-lactamase inhibitors	17,18,23,24,27,28
Chronic underlying disease, previous hospitalization	A variety of conditions cited but may reflect regular contact with healthcare and/or exposure to antibiotics	16,20
Extrinsic		
Intensive care unit	Many studies on risk factors focus on intensive care unit rather than all hospital patients	17
Transfer from LTCF	May reflect underlying disease and lack of focused preventive measures in LTCF	17
Previous patient in single room, VRE positive	May reflect inadequate terminal decontamination	21,22
Prior hospitalization/transfer from another hospital	Many studies carried out in larger referral hospitals receiving patients from other institutions	19

LTCF, long-term care facility.