Screening, Isolation, and Decolonization Strategies for Vancomycin-Resistant Enterococci or Extended Spectrum Beta-Lactamase-Producing Organisms: A Systematic Review of the Clinical Evidence and Health Services Impact

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Introduction

Bacterial resistance to antibiotics is an increasing problem in Canada and worldwide.[1-4] Vancomycin-resistant enterococci (VRE) are strains of *Enterococcus faecium* or *Enterococcus faecalis* that contain genes conferring resistance to vancomycin.[5,6] *Escherichia coli* (*E. coli*), *Klebsiella pneumonia* (*K. pneumonia*), and other gram-negative bacteria may produce the enzymes known as extended spectrum beta-lactamases (ESBLs). These have the ability to inactivate beta-lactam antibiotics such as penicillin, ampicillin, and the cephalosporins.[7,8]

The presence and growth (colonization) of VRE and ESBL-producing micro-organisms in the gastrointestinal tract is usually of no consequence for the host; but under certain circumstances — such as immunosuppression, gastrointestinal surgery, or physical debilitation — they may serve as a source of infection for the carrier. These hosts may also serve as a reservoir for the transmission of VRE and ESBL-producing organisms to other persons.[9,10]

Results from the Canadian Nosocomial Infection Surveillance Program showed that, from 1999 to 2005, the rate of VRE colonization and VRE infection increased from 0.37 to 1.32 cases, and from 0.02 to 0.05 cases, respectively, per 1,000 patients admitted to hospital.[11] The laboratory-based Canadian Ward Surveillance Study in 2008 found that ESBL-producing *E. coli* were identified in all Canadian geographic regions, and that 4.9% of *E. coli* isolates were ESBL producers.[12]

Specific prevention and control measures for antibiotic-resistant organisms (AROs) include screening (a process to identify persons colonized with AROs) and isolation of the carriers. Hospital infection prevention and control strategies have been developed in some Canadian jurisdictions,[13-16] and these are compatible with other national and international documents.[17,18] Non-specific strategies for controlling ARO transmission and infection include hand hygiene, environmental cleaning, antimicrobial stewardship, and bundled practices such as those to prevent central line-associated blood stream infections.

Antibiotic-resistant organisms, such as VRE and ESBL-producers, lead to the increased use of hospital resources due to extended hospital stays, laboratory tests, physician consultations, medications if a VRE or ESBL-related infection were to arise, and the need to adhere to infection prevention and control measures to prevent the further spread of these pathogens.[19] Some of the increased resource usage results from the morbidity caused by VRE or ESBL-producing organism infections, while some is a consequence of control strategies. For example, it may be harder to transfer a patient to a rehabilitation facility if the patient is currently in isolation, which will in and of itself prolong the length of stay.

The objective of this systematic review is to evaluate the clinical evidence for the effectiveness of screening, isolation, and decolonization strategies for persons colonized or infected with VRE and ESBL-producing organisms in acute and long-term care facilities. The health services impact of these strategies will be discussed.

Objective

The objective of the report is to answer the following research questions:

1. What is the clinical evidence on the effectiveness of selective versus universal versus no screening of patients (adult and pediatric) for VRE or ESBL-producing organisms?
2. What is the clinical evidence on the effectiveness of patient isolation for VRE or ESBL-producing organisms?
3. What is the clinical evidence on the impact of isolation on the patient?
4. What is the clinical evidence for the effectiveness of decolonizing patients known to be carrying VRE or ESBL-producing organisms?
5. What is the clinical evidence on the effectiveness of additional precautions in the operating room or post-anesthesia recovery room in patients colonized with VRE or ESBL-producing organisms?
6. What is the health services impact of screening, isolating, and decolonizing patients known to be carrying VRE or ESBL-producing organisms on blocked beds, cancelled or limited surgeries, or the range of services a facility can provide?

Methods

For the clinical evidence, an information specialist performed the literature search using a peer-reviewed search strategy. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and non-randomized studies. Trials were eligible for inclusion if they involved adults or pediatric patients in acute or long-term care facilities, with VRE or ESBL-producing organisms; compared the effectiveness of screening, isolation, and decolonization with no screening, no isolation, and no decolonization; and reported outcomes related to detection, transmission, and infection of VRE or ESBL-producing organisms.

The information specialist also conducted a search on the health services impact of the related main search concepts, using the same methodology as for the clinical evidence. Trials were eligible for inclusion if they involved adults or pediatric patients in acute or long-term care facilities with VRE or ESBL-producing organisms and discussed the impact of screening, isolation, and decolonization of these patients on hospital resources.

Regular alerts were established to update the search until the publication of the final report.

Grey literature (literature that is not commercially published) was identified by searching relevant sections of the Grey Matters checklist (http://cadth.ca/resources/grey-matters).

Results

Observational studies showed that active surveillance with weekly rectal swabs in high-risk units was associated with lower VRE bacteremia rates compared with no surveillance strategy. Compared with isolates in a hospital

without active surveillance, an active surveillance program was associated with a population of VRE that is more polyclonal (i.e., having genetically different origins), which may be evidence of less person-to-person transmission of the organism. In situations where routine infection prevention and control measures fail to prevent the transmission of ESBL-producing organisms — that is, during a clonal outbreak — an aggressive control strategy may be effective, with daily surveillance cultures, increased contact precautions, and staff reinforcement regarding the use of precautionary measures. The implementation of guidelines in hospitals, to ensure strict isolation plus contact precautions, was shown to be important in controlling the spread of VRE colonization. Contact precautions and isolation, however, may have a negative psychological impact on patients, seen in increased rates of depression and anxiety. There was no evidence found on the clinical effectiveness of decolonization compared with no decolonization on VRE and ESBL-producing infection and transmission.

Evidence from retrospective cohort studies suggested that patients infected with hospital-acquired VRE or ESBL-producing organisms have a longer length of hospital stay than matched cohorts of control patients. Prolonged lengths of stay were due to a variety of reasons, which included the infection itself, improper administration of initial antibiotic therapy, or infection prevention and control measures used to prevent the spread of infection to other patients. This increased length of stay contributes to increased use of hospital resources, such as blocked beds and rooms, and the need for more health care worker time providing direct patient care.

Limitations

Clinical Assessment

There are few reports on which to make evidence-based conclusions, and the ones that were identified had significant methodological concerns. There was only one outbreak study on which to base findings on the effectiveness of surveillance and contact precautions for ESBL-producing organisms, which is insufficient from which to draw firm conclusions. There was no evidence found that compared the effectiveness of decolonization with non-decolonization for patients carrying VRE or ESBL-producing organisms.

The main limitations of all the studies were the lack of randomization and blinding, which increase the potential for bias; size of the included populations; and the inability to determine if confounders were considered in case and control groups in most studies (two on VRE, one on ESBL-producing organisms, and one on depression).[20-23] Additionally, two studies on VRE collected data from the cohorts at different time periods,[21,24] and two studies on anxiety and depression did not indicate if the same time periods were examined for the patient groups.[22,25]

Health Services Impact Assessment

Due to the limited number of studies identified (n = 4), it is difficult to draw definitive conclusions regarding the health services impact of screening, isolating, and decolonizing patients known to be carrying VRE or ESBL-producing organisms. In addition, all of the studies were observational studies from single institutions, which may limit the generalizability of the results. The specific population in the studies may not be representative of all hospitals. Observational studies may also be prone to bias and confounding, as researcher

bias can influence both the design of a study or data collection. The retrospective nature of these studies may also be prone to bias and confounding, as both outcomes and exposures have already been established at the time of participant selection.

Conclusions

Although there are few reports upon which to formulate evidence-based conclusions, evidence from a limited number of observational studies with methodological concerns showed that active surveillance (screening of all high-risk patients), patient isolation, and specific precautionary measures in hospital settings may result in reducing the spread and colonization of, and infection with, VRE and ESBL-producing organisms. Increased rates of depression and anxiety were seen in patients under strict isolation and contact precautions. Stronger evidence, supported by adequately powered, multicentre cohort studies with robust analyses to minimize the potential biases, is needed to confirm these findings. There was no evidence found that compared the effectiveness of decolonization with non-decolonization of patients carrying VRE or ESBL-producing organisms. Decolonization is not typically performed for patients with VRE or ESBL colonization.

As transmission risk was shown to be associated with the number of roommates, the design of acute care hospitals is important to minimize the transmission risk. Deployment of staff is important to focus the attention on high-risk units. Direct and efficient communication between different teams is also a necessity. With foreign travel identified as an infection transmission risk factor, it is important that medical practitioners be aware of the infection risk in returning travellers. Implementation of precautionary measures must take into consideration the negative psychological effects that isolation may have on hospitalized patients.

Observational studies showed that patients infected or colonized with VRE or ESBL-producing organisms use more hospital resources because of the increased length of their stay in the hospital, increased usage of hospital beds, increased health care worker staffing, and the need for precautions to prevent the spread of infection. Although infection prevention and control measures may be effective at preventing the spread of these organisms, there is a lack of evidence regarding whether or not these are cost-effective measures; and practice is variable.

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