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SHORT COMMUNICATION

Vancomycin-resistant *Enterococcus faecium*: should we screen on admission?

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Denmark has experienced an increase in the proportion of invasive vancomycin-resistant *Enterococcus faecium* (VRE) since 2002 (*e.g.* <4% in 2015, 7.1% in 2017 and 12% in 2018). At Rigshospitalet, we employ active screening at departments with high prevalence or in case of outbreaks. This includes the collection of rectal swabs specifically for VRE screening. Our purpose was to describe the carrier prevalence of vancomycin-resistant enterococci among acute patients admitted to the Neurointensive Care Unit, Department of Neuroanaesthesiology, Rigshospitalet, Copenhagen, Denmark (NICU). Between April 2018 and January 2019, we investigated 99 consecutive rectal swabs from patients admitted to NICU. The primary outcome was prevalence of VRE carriage. The median age was 64 years (range 23–87) and gender was equally distributed (Female = 47, Male = 46). 26 (28%) had previously been admitted within 179 days and 67 patients (72%) had no hospital admissions within 180 days prior to the admission to NICU. Of the 93 rectal swabs, 2 (2%, 95% CI 0.26–7.55%) were positive for *vanA* and none were positive for *vanB*. Routine screening of all patients at admission may be effective in hospital settings with high VRE prevalence, whereas the benefit of screening for VRE in hospitals with a low prevalence may be restricted to specific patient populations.

Key words: VRE; active screening; bacteriology; clinical microbiology; multidrug resistance.

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Denmark has experienced an increase in the proportion of invasive vancomycin-resistant *Enterococcus faecium* (VRE) since 2002 (*e.g.* <4% in 2015, 7.1% in 2017 and 12% in 2018) (1). This proportion of invasive VRE is relatively high, especially when we compare ourselves to the other Nordic countries that have a range of 0–2.3% (1). We rarely see *E. faecalis* isolates resistant to vancomycin and/or ampicillin (0.2% and 0.2%, respectively) (1), which is why *E. faecium* is of importance in the context of vancomycin resistance only (1).

Southern European countries like France and Spain have lower percentages of invasive VRE than Denmark. However, the European Antimicrobial Resistance Surveillance Network which is a part of The European Centre for Disease Prevention and Control did report a worrisome increase in VRE in several countries in the European Union/European Economic Area, from 10.5% in 2015 to 18.3% in 2019 (EARS-Net annual report, 2019). At Rigshospitalet, Copenhagen, Denmark, several intensive care units (ICUs), including Department of Neuroanaesthesiology (NICU), have had a high prevalence of patients carrying VRE. Prompt identification of colonized patients combined with effective infection control practices and antimicrobial stewardship programs to reduce the selection of VRE, can decrease the transmission and help prevent hospital-acquired infections (1–3). As such, screening of patients is also a tool to terminate the use of unnecessary contact precautions. However, the optimal approach to screening is still debated (3,4). At Rigshospitalet, we employ active screening at departments with high prevalence or in case of

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outbreaks (3). This includes the collection of rectal swabs specifically for VRE screening.

Well-documented treatment options for VRE are linezolid, tigecycline and daptomycin (5,6). Consumption of linezolid increased 1.5-fold from 2010 to 2019 at Rigshospitalet, and linezolid has a high risk of potential adverse effects as well as development of resistance in *E. faecalis*, *E. faecium* and Coagulase-negative Staphylococci (unpublished data from Rigshospitalet) (1). The Capital Region of Denmark accounted for 73% of the consumption of linezolid in Denmark in 2019, likely due to the increasing prevalence of VRE (1).

From 2002 until 2018, vancomycin resistance was almost exclusively found in *E. faecium* isolates carrying *vanA*. However, since 2018–20, VRE isolates carrying v*anB* are becoming more prevalent (1). Finally, in recent years, *E. faecium* harbouring *vanA* complex, but phenotypically susceptible to vancomycin, has been described (1). These enterococci are referred to as vancomycin-variable enterococci (VVE) and are equally clinically relevant. Therefore, their detection is critical in order to avoid treatment failure with vancomycin (1). Consequently, all invasive isolates at Rigshospitalet are tested for the presence of *vanA*/*vanB* by polymerase chain reaction (PCR).

The purpose of this study was to describe the carrier prevalence of VRE among acute patients admitted to the Department of Neuroanaesthesiology, Rigshospitalet, in Copenhagen, Denmark. The primary outcome was the prevalence of VRE carriage.

METHODS

This was a single-centre study performed at NICU and the Department of Clinical Microbiology (DCM) Rigshospitalet, Copenhagen, Denmark, only.

Between April 2018 and January 2019, we investigated 99 consecutive rectal swabs from patients admitted to NICU. All patients were eligible for inclusion if they were ≥18 years. All participants delivered one baseline rectal swab (a welcome screening) performed at admission, prior to initiation of antimicrobial treatment.

Six samples were lost during transfer to the DCM or were leaking at the time of arrival, and thus, were discarded; the patients providing these samples were excluded. Thus, a total of 93 samples from 93 patients were analysed.

The algorithm for VRE screening of rectal swabs was as follows: all rectal swabs were screened for *vanA*/*vanB*/*vanC* using the commercially available system "The BioGX Vancomycin Resistance – OSR for BD MAX™" and BioGX reagents (Becton Dickinson Denmark A/S, Lyngby, Denmark). *vanB*-positive samples were cultured on a selective BD selective CHROMagar (Becton Dickinson Denmark A/S, Lyngby, Denmark). Growth of an *E. faecium* or *E. faecalis* was interpreted as VRE. No growth of an *E. faecium* or *E. faecalis* was interpreted as negative for VRE despite a positive PCR. Antimicrobial susceptibility testing was mainly performed by disc diffusion. In brief, the samples analysed are complex rectal swabs, and hence, include many different species. *VanA* is only found in *Enterococcus* species, whereas *vanB* can be found in anaerobes as well, with no clinical impact. A positive PCR could mean that the gene is present in another species than Enterococci. Therefore, the PCR is always followed by culturing. By culturing on a VRE plate with 4 μg/mL vancomycin, we confirm vancomycin-resistant Enterococci.

RESULTS

The median age was 64 years (range 23–87) and gender was equally distributed (Female = 47, Male = 46).

Twenty-six (28%) had been previously admitted within 179 days and 67 patients (72%) had no hospital admissions within 180 days prior to the admission to NICU.

Of the 93 rectal swabs, 2 (2%) were positive for *vanA* (95% CI 0.26–7.55%) and 36 were positive for *vanB* (39%). Both patients positive for *vanA* had been admitted to a hospital within the previous 30 days. From 7 of the 36 *vanB* positive rectal swabs only, we were able to culture *Enterococcus* spp. on selective agar with vancomycin (1 *E. gallinarum*, 1 *E. faecium* and 5 *E. faecalis*). Confirmatory PCR on these isolates showed one *E. gallinarum* carrying *vanC* and negative results for the remaining 6 isolates. Furthermore, 10 patients were screened for VRE during hospital admission, and all were found to be negative. One excluded patient was diagnosed to carry VRE (*vanA*) during hospital admission. Thus, we found that 2 patients out of 93 patients (2%; 95% CI, 2.6–7.6%) carried VRE (*vanA*) at the time of admission to a tertiary hospital and a highly specialized intensive care department. Both had previous hospital admission within the past 30 days, but none had been hospitalized abroad. Of note, of 26 patients with recent hospital admission, two (15%; 95% CI, 9.5–25.1%) carried VRE.

DISCUSSION

Active screening is the collection of specimens specifically for VRE screening while passive screening relies on detection of VRE from clinical specimens. Active screening often includes testing upon hospital admission (3), and is performed mainly to protect VRE-free patients (4). Admission screenings have been proposed to stop the ongoing spread of VRE. A recent Danish study aimed to describe the carrier prevalence of four different multidrug-

resistant bacteria (MDR) among acute patients in Danish emergency departments (EDs) (7): methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenemase-producing enterobacteria (CPE), extended-spectrum beta-lactamase-producing enterobacteria (ESBL) and vancomycin-resistant enterococci (VRE) (7). The study included 5117 patients in the study and 266 were colonized with at least one MDR, with a VRE prevalence of 0.4% (7). Furthermore, colonization rates for inpatients range from as low as <2% in Finland to as high as 34% in Ireland (3).

The presumption that we can prevent outbreaks relies on the optimal adherence to isolation (4). Currently, it is assumed that isolation is 75–80% effective in reducing transmission (4). Additionally, other studies found that active VRE screening and isolation resulted in detection of 82%–91% of VRE carriers (4). Mac *et al*. (4) used a mathematical model to predict that active screening contributed to a reduction of six cases of VRE colonization's over 1000 admissions and isolation strategies reduced the number of VRE-related bacteraemia events by 2/10,000 patients. This is to be balanced against cost of private/single-bed hospital rooms and the (7,8) maximum capacity of wards (4). Thus, active screening programs have an effect, but we need to obtain more sophisticated VRE surveillance data to implement active screening wisely. We likely need annual or bi-annual prevalence studies to clarify the need for welcome screenings—as well as longitudinal screening studies on admitted patients to evaluate time of colonization. Active screening and longitudinal screening studies may be tools for antibiotic stewardship programs to avoid redundant use of linezolid. Finally, it would be interesting and relevant to compare screening strategies and hospital transmission rates of VRE between areas of low prevalence with data from a high-prevalence setting. Currently, one Region in Denmark has stopped screening for VRE as well as infection control practices, such as patient isolation. Data from this Region will be interesting to follow. We believe active screening of selected populations may still be relevant, such as screening of patients who have been hospitalized abroad, patients previously found to be VRE-positive or patients previously admitted to departments with high VRE-prevalence (7,8).

CONCLUSION

With a very low prevalence of VRE, a universal admission-screening program appears neither cost-beneficial nor necessary for patient safety. Yet, for patients with recent hospital admission, notably patients who have been admitted to departments with high prevalence or during existing outbreaks, active screening should be promoted to stop outbreaks and avoid carriers transmitting VRE to patients and staff. This could include active screening before transfer to another department or at re-admission within six months of a hospital discharge. Thus, routine screening of patients at admission may be effective in hospital settings with high VRE prevalence but may not be justified in hospitals with a low prevalence (3,4).

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CONFLICT OF INTEREST

Frederik Boetius Hertz have received honoraria from B. Braun Medical A/S and Triggerz ApS. The remaining authors have no conflicts of interest to declare.

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