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Acute vancomycin-resistant enterococcal bacteraemia outbreak analysis in haematology patients: a case-control study

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Abstract. ***Introduction*:** We report a retrospective case-control series of a vancomycin-resistant *Enterococcus faecium* (VRE) bacteraemia outbreak at a tertiary metropolitan hospital in Queensland, Australia. The outbreak occurred on a haematology ward between 8 and 14 February 2014, 6 weeks after a ward relocation. The aim was to determine risk factors related to progression from colonisation with VRE to bacteraemia.

***Methods*:** The cases were patients with haematological malignancy and proven catheter-related VRE bacteraemia. Matched controls were selected from the same ward with similar underlying haematological diagnoses and proven gastrointestinal VRE colonisation without invasive infection.

***Results*:** This study suggests that female sex, recent administration of total parenteral nutrition, right-sided catheter placement with odds ratios (OR) 1.99, gastrointestinal disruption (OR: 1.91), and dexamethasone administration (OR: 2.37) are potential risk factors for progression from colonisation to infection. Notably, given the small sample size, the 95% confidence intervals are wide ranging from 0.02 to 222.

***Conclusion*:** While progression from colonisation with VRE to invasive disease is likely to be a complex multifactorial process, the results of this study suggest certain clinical variables that warrant enhanced vigilance to reduce this occurrence. Interestingly, recent relocation of the haematology ward may play a significant role in this outbreak. This study highlights the importance of good infection control practice and the need for additional studies to further delineate risk factors for invasive VRE infection.

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Introduction

Vancomycin-resistant enterococci (VRE) were first isolated in Australia from a liver transplant recipient in Melbourne in 1994[1] and first reported in Queensland in 1996.[2] The epidemiology of VRE in Australia is different from that reported elsewhere, with VanB *Enterococcus faecium* predominating.[3]

Since the 1990s, the incidence of VRE in Australia has escalated dramatically. Comparison of nationwide surveillance studies in Australia has shown an increase in the prevalence of VRE amongst enterococcal isolates causing disease, from 16.4% in 2007 to 36.5% in 2010 and up to 40.9% as recently as 2013.[4] At the Mater Hospital, the rate of colonisation has increased from 0.35 per 1000 occupied bed days (OBD) in 2010

Implications

- This report is unique in that it describes a significant increase in invasive infection in a very short space of time in a single location, enabling further analysis of potential contributing factors.
- Given the morbidity and mortality of vancomycin-resistant enterococcus bacteraemia, adequate infection control practices and risk minimisation are imperative. Further work in this area is herein able to be suggested on the basis of the findings reported.
- Whilst currently still a relatively rare event, invasive infection with vancomycin-resistant enterococcus is likely to increase on the basis of increasing rates of colonisation, and further research regarding preventing progression to invasive infection as is reported here is required.
- This is the first publication to associate ward relocation and a bacteraemia outbreak.

to 3.49 per 1000 OBD in 2014.The rates of VRE bacteraemia at our facility have increased from <0.1 per 1000 OBD in 2010 to 0.14 per 1000 OBD in 2013. However, the average number of VRE bacteraemia cases at our facility is approximately two per year. Screening is only carried out on patients admitted to our intensive care units (ICUs) and haematology/oncology wards. This practice has not changed between 2010 and 2014, and therefore does not account for the increased incidence.

Vancomycin resistance in *E. faecium* bacteraemia isolates ranges from 5 to 35% in Europe to 60% in North America.[5] In an Australian study, 56% of *Enterococcal* bacteraemia isolates are *E. faecalis*, 38.5% *E. faecium*, and the remaining 5.4% consist of *E. casseliflavus*, *E. gallinarum*, *E. avium*, *E. hirae*, *E. raffinosus*, *E. durans* and *E. gilvus.* Notably, as of 2013, 40.9% of the *E. faecium* isolates were vancomycin-resistant, and only one *E. faecalis* isolate (0.2%) was vancomycin-resistant.[4] These findings are similar to those reported in North America and Europe. In the International SENTRY Program, *E. faecalis* is the most frequently isolated enterococcal species at 61%, followed by *E. faecium* at 5–19%. Furthermore, *E. faecium* accounts for 93% of VRE isolates in North America and 74.1% in Europe.[6]

The reason for concern regarding enterococci is due to their intrinsic resistance to multiple antimicrobial agents and their ability to acquire and potentially propagate resistance via the transfer of plasmids and transposons.[7] Internationally, hospital-associated *E. faecium* isolates are known to be part of a specific clonal lineage, clonal cluster 17 (CC17), that has successfully adapted to hospital environments. CC17 is ampicillin- and quinolone-resistant and is able to acquire the VanA- or VanB-containing transposons via horizontal gene transfer.[8] In certain settings, the rate of VRE colonisation may be as high as 50%.[9] Worldwide, VanA is the most common VRE genotype, but in Australia VanA accounts for 6.1% of bacteraemia isolates, while VanB isolates, that are usually sensitive to teicoplanin, predominate.[10,11]

Internationally, VRE accounts for ~10% of all bacteraemia cases.[5] Recent Australian data estimates that VRE bacteraemia accounts for 15% of all bacteraemia cases.[4] In our facility the average rate of VRE bacteraemia was 2.5 per year between 2010 and 2013. However, in February 2014, four cases of VRE bacteraemia occurred in less than 1 week; therefore an anomalous and important event. While there have been several hospital outbreaks of VRE in Australia, these are mostly outbreaks of colonisation. To our knowledge, this was the first outbreak of hospital-acquired VRE bacteraemia to occur over such a short period of time. We report the results of a case-control study of the patients who developed VRE bacteraemia at our institution during this outbreak, with a view to identifying risk factors for progression from colonisation to invasive infection in order to focus subsequent actions towards risk reduction.

Materials and methods

The VRE outbreak occurred in a tertiary metropolitan hospital in Queensland, Australia. The Mater hospital has two haematology/oncology units; the one described in this study has 30 beds. The presence of VRE *faecium* was confirmed in the blood cultures of four patients between 8 and 14 February 2014. All four patients were undergoing chemotherapy for haematological malignancy and were located in the same ward. This outbreak occurred approximately 6 weeks after relocation of the haematology/oncology inpatient services to a different ward. Ethics approval was granted by the Mater Hospital ethics committee.

The cluster of VRE positive blood cultures over a short space of time from the same haematology ward alerted our facility's infection control team. An outbreak control team was created in order to halt the spread of VRE and limit the number of patients with bacteraemia. This team involved the infectious diseases physicians, clinical microbiologists, infection control unit, heads of department for nursing, hotel services (including cleaning and catering), and hospital management.

Data on the patients with invasive infection were collected to inform the outbreak control team of possible aetiological factors. In order to clarify risk factors for invasive disease in the four cases, all known VRE colonised patients in the unit were identified and used as controls. They did not have any invasive VRE infection, defined as no microbiological evidence of VRE in clinical samples including blood, cerebrospinal fluid, pleural fluid, pericardial fluid, synovial fluid or at surgical sites, and all VRE patients were isolated in single rooms.[12]

The cases and controls were compared for all factors including age, sex, underlying malignancy, intravenous access (type, location, number of lumens and dwell time), duration of colonisation, duration of hospitalisation, duration of neutropenia, gastrointestinal disturbance as well as antibiotic use within the preceding month.