Short Report

Journal of Infection Prevention

Journal of Infection Prevention
2017, Vol. 18(3) 149–153

DOI: 10.1177/1757177416687832
jip.sagepub.com
SAGE

Outbreak of vancomycin-resistant *enterococcus* on a haematology ward: management and control

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Abstract

Vancomycin-resistant enterococci (VRE) infections and outbreaks are still infrequent in Spain. A six-month outbreak, which took place in a haematology ward, its control and management are described in this study. A total of 22 patients were colonised and two bloodstream infections occurred during this period. Even though there were two waves of new colonised patients, a multidisciplinary approach, quick interventions and enhanced infection control policies were required in order to control this outbreak.

Keywords

Antimicrobial drug resistance, healthcare-associated infections, Enterococcus, vancomycin

Date received: 19 April 2016; accepted: 14 December 2016

Introduction

Enterococci remain one of the most frequent in community-acquired and nosocomial infections. The high incidence of vancomycin-resistant enterococci (VRE) in the United States has been attributed to the widespread use of vancomycin in USA hospitals, while vancomycin consumption was lower in Europe (Van Boeckel, 2014). Nevertheless, European Union/European Economic Area population-weighted mean percentage for vancomycin resistance in *E. faecium* has shown a significantly increasing trend over the last four years, being 8.9% in 2013, although this figure remains lower in Spain (0.9%) and outbreaks are infrequent. The change from a stable situation regarding VRE may indicate changes in the epidemiology of VRE in Europe (European Centre for Disease Prevention and Control, 2013).

Enteroccocci are bacteria that are normally present in the human intestines and in the female genital tract and are often found in the environment. Clinical infections caused by *Enterococcus* include urinary tract infections, bacteraemia, bacterial endocarditis, diverticulitis, pneumonia and meningitis. High-risk patients' colonisation by VRE usually precedes infection, resulting in greater mortality, longer hospital length of stay and higher associated costs. The ability of enterococci to survive outside the human body is crucial to its spread among patients, either via hands, surfaces or equipment (Lode, 2009).

In order to control outbreaks caused by VRE, active surveillance cultures of patients in the unit, rapid detection of new cases and their molecular classification are mandatory, in addition to emphasising infection control precautions (Siegel et al., 2006)

This paper reports an outbreak of VRE in a Haematology Unit of a Spanish teaching hospital and the key points of its management and control.

Materials and methods

The outbreak lasted from mid-February to July 2015, in a 27-bed Haematology Unit (12 double and three individual

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rooms) of a tertiary hospital in Tenerife, Canary Islands, Spain. This 650-bed hospital provides a service to a total population of 430,000. The Infection Control Unit is staffed with three medical specialists and five trained nurses. The outbreak was triggered by two patients who presented with VRE bloodstream infections. The case definition was a patient with VRE isolated from clinical or screening samples.

Ethical approval and patient consent was not required for management of the outbreak, as procedures followed hospital policy.

After the onset of the outbreak in the Haematology Unit, active surveillance cultures looking for VRE were carried out once a week on all patients admitted to this unit. Rectal swabs were plated directly onto chromID VRE (bioMérieux, Marcy l'Étoile, France), presumptive colonies were tested by vitek GP (identification), AST-589 card (antimicrobial susceptibility), and vancomycin and teicoplanin E-tests.

Contact precautions (use of gloves and aprons while in contact with a patient or their surroundings) were implemented for all patients diagnosed with VRE, both infected and colonised, and they were isolated in single rooms or cohorted in same room if possible (according to gender and clinical situation of these patients, coordinated by nursing staff in the unit and infection control staff). These rooms have en-suite bathrooms.

The hospital Board of Directors and the Head of Unit were informed and groups were organised to train unit staff on measures to prevent nosocomial transmission of infection. Seven 1-h training sessions were delivered by Infection Control Unit staff to 22 people (five doctors, ten nurses and seven nursing assistants), consisting of infection control procedures that included hand hygiene, patient washing and contact precautions, following the CDC recommendations (Siegel et al., 2006).

The frequency of environmental decontamination of the unit was also increased to twice a day with chlorine releasing agents (500 ppm), degradable equipment was cleaned with quaternary ammonium germicidal detergent solution, and patient washing daily with chlorhexidine was introduced until the outbreak was over, following the CDC guidelines (Rutala et al., 2008). All visitors were aware of requirements as they were informed by nursing staff before entering the room. Protocols of empirical use of glycopeptides were also reviewed by antimicrobial stewardship staff.

Vancomycin-resistant gene typing was performed by specific polymerase chain reaction (PCR) as previously described (Bell et al., 1998).

The relationship between the different strains was established by Pulsed-Field-Gel-Electrophoresis (PFGE), digested with *Sma*I (Promega Corporation, Madison, WI, USA), and restriction patterns were interpreted by Tenover criteria (Tenover et al., 1995).

Results

Outbreak description

The index case was an 80-year-old woman with multiple myeloma who developed a primary blood stream infection (BSI) with *Candida albicans* and VRE two months after her admission. She was treated with linezolid and caspofungin, and, after clinical recovery in the first few days, her condition deteriorated and she died four weeks after the BSI.

The second infected patient, a 60-year-old woman with acute promyelocytic leukaemia, was diagnosed with a BSI secondary to pneumonia by VRE one month after hospitalisation. She was successfully treated with linezolid and discharged two weeks later.

Active surveillance of the unit detected 11 additional cases of rectal colonisation in the first three weeks. After control measures were implemented, the incidence of new colonised patients decreased. Then, in June, a second transmission peak occurred (Figures 1 and 2).

After the first three weeks of active surveillance, surface cultures of the unit were performed in both VRE-positive and non-positive patients' rooms. Overall, 38 different objects inside the patients' rooms were cultured (bedside tables, wheelchairs, toilet chairs, sofas and bed handrails). Only one bed handrail was found to be positive for VRE, from the bed of one of the previously known colonised patients.

After 29 weeks of continuous surveillance, and with no new cases in 1.5 months, the outbreak was declared over, although rectal swabs continued to be taken monthly. No additional cases were detected in the unit. Previously colonised patients are cared for with contact precautions when admitted to hospital, as identified in their clinical history. During the six months that the outbreak lasted, 117 patients were screened for VRE, with 22 identified as positive.

Empiric use of glycopeptides was restricted. Until the outbreak, every patient with a central catheter with febrile neutropenia was treated with a beta-lactam and vancomycin. Following this review, vancomycin was only added for clinically unstable patients.

Microbiology and molecular analysis

In total, 22 patients were positive for VRE from rectal swabs during the outbreak; in two of these patients, VRE was also recovered from blood cultures. All were identified as *E. faecium* and reported as resistant to vancomycin by Vitek-2 AST-589 card, results confirmed by E-test (vancomycin MIC >256 mg/L in all strains). Resistance to teicoplanin was reported in all isolates, with MIC by E-test in the range of 32–64 mg/L. All isolates remained susceptible to linezolid and did not have high-level gentamicin resistance.

PCR revealed that all isolates carried the *vanA* gene. Three closely related restriction patterns were found by PFGE analysis.

Figure 1. Outbreak evolution of the new colonised cases and their incidence during six consecutive months. A1, A2 and A3 represent the different subtypes of PFGE patterns found.

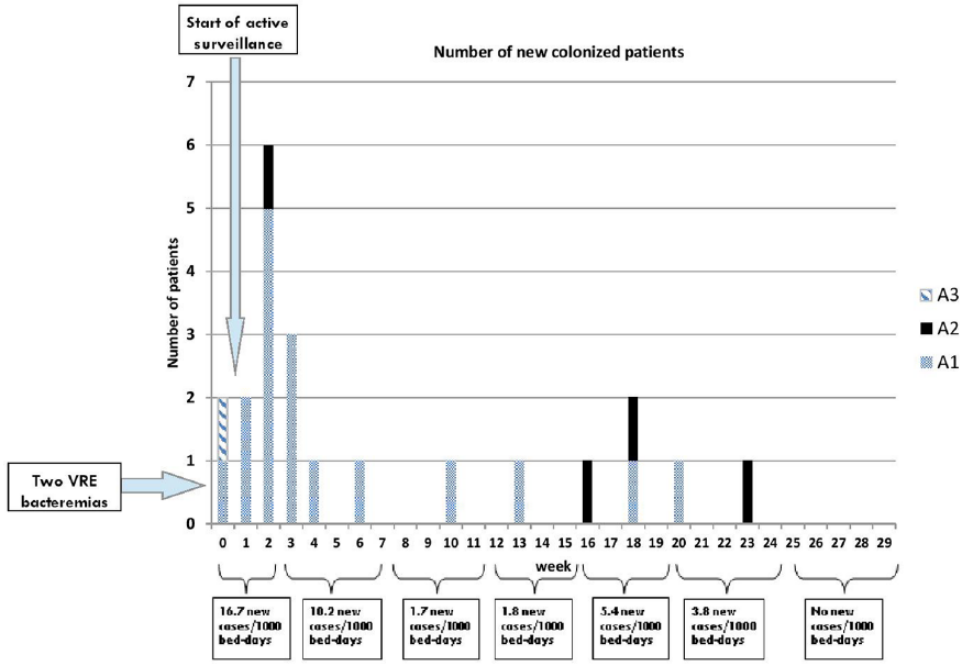
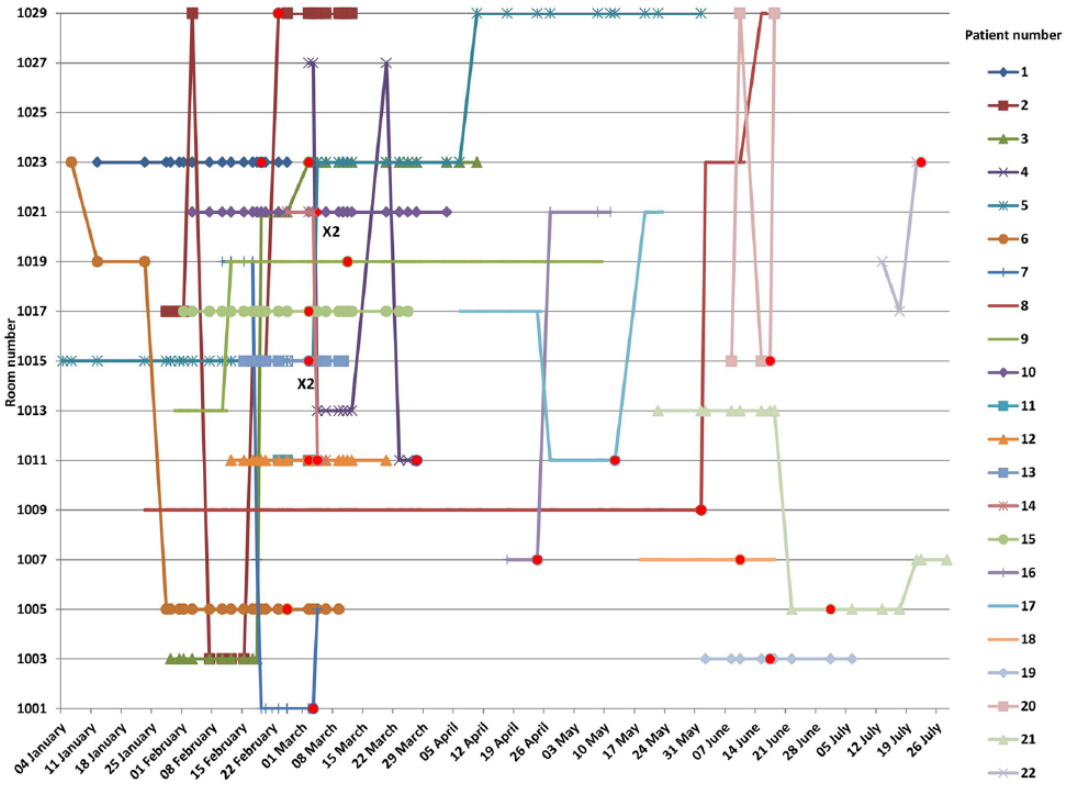


Figure 2. Timeline representing movements of the VRE colonised patients in the Haematology Ward. Red dots indicate VRE detection.



Discussion

Patients with onco-haematological diseases are prone to colonisation by multidrug-resistant microbes (MDR). Long stays in hospital, as well as frequent and multiple antimicrobial treatments, are risk factors linked with the acquisition of MDR. In the case of VRE, vancomycin use, prolonged hospitalisation, severe underlying conditions and invasive devices are among the risk factors that have been strongly associated with the colonisation of these patients (Ford et al., 2015; Humphreys, 2014).

In the Canary Islands, as in the rest of Spain, *vanA* VRE outbreaks are very uncommon. In 2005, there was another outbreak linked to this hospital, but in the Nephrology Ward. It resolved in just three months with four infections and 12 colonisations (Montesinos et al., 2010). An outbreak has also been described in the southern part of Spain, affecting 13 patients of the Haemo-oncology Ward, there were seven infections and six colonised patients (Valdezate et al., 2012), with similar management including infection control procedures and patient sampling frequency.

Active surveillance of the unit, as well as infection control precautions, were essential to reduce and, eventually, stop the spread of VRE among these patients. As described in other papers, there are many actions that enable the control of VRE outbreaks (Humphreys, 2014). Enhanced adherence to hand hygiene, infection control precautions, education, patient cohorting and good communication between the Haematology and Infection Control Units were among the measures taken. Controlling the empiric use of the glycopeptides was an important factor in controlling this outbreak and following this change in practice, new colonisations were not detected for six consecutive weeks.

Although there are other techniques for typing VRE, PFGE still has the most discriminative power in comparisons (Chuang et al., 2010). Rep-PCR has shown a better turnaround time, but the PFGE typing method, with its reduced cost and long-time experience, continues to be the gold standard for describing outbreaks. All VRE strains described in this paper were closely related, indicating that a common source is possible.

However, there are some limitations in this report. Importantly, it has not been possible to find the source of the outbreak and, although one strain was recovered from the environmental cultures, this is insufficient evidence to indicate a causal link. Additionally, no hand hygiene and antimicrobial prescribing audits were performed after the training sessions, making their impact more difficult to analyse.

Among the lessons learned, performing audits after training, reviewing the empirical use of glycopeptides and rapid establishing of infection control procedures should be highlighted.

In conclusion, there are several procedures to control a VRE outbreak in a haematology unit. Molecular typing and infection control activities described above remain the most important. Although no new infections occurred after the first two bacteraemias, with the control of colonised patients it has been possible to prevent new cases of VRE colonisation, and infection.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Peer review statement

Not commissioned; blind peer-reviewed.

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