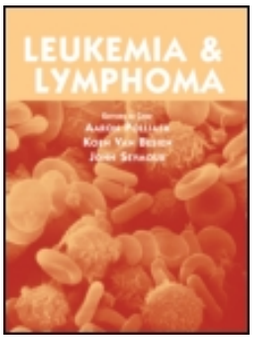

Leukemia & Lymphoma

ISSN: 1042-8194 (Print) 1029-2403 (Online) Journal homepage: informahealthcare.com/journals/ilal20

Vancomycin-resistant enterococci in patients with hematological malignancy: curbing an endemic pathogen

Leon J. Worth

To cite this article: Leon J. Worth (2014) Vancomycin-resistant enterococci in patients with hematological malignancy: curbing an endemic pathogen, Leukemia & Lymphoma, 55:6, 1225-1226, DOI: 10.3109/10428194.2013.845887

To link to this article: https://doi.org/10.3109/10428194.2013.845887

Leukemia & Lymphoma, June 2014; 55(6): 1225–1226

ISSN: 1042-8194 print / 1029-2403 online
DOI: 10.3109/10428194.2013.845887

informa
healthcare

COMMENTARY

Vancomycin-resistant enterococci in patients with hematological malignancy: curbing an endemic pathogen

Leon J. Worth

Department of Infectious Diseases and Infection Prevention, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia

During the past three decades, vancomycin-resistant enterococci (VRE) have emerged as significant pathogens in hospitalized patients. Initially associated with outbreaks in healthcare settings [1], VRE are now recognized as endemic pathogens in many centers, including immunocompromised patient populations admitted to nephrology and intensive care units, as well as hematology and bone marrow transplant populations. Endemic VRE subtypes vary according to geography and local epidemiology, with *Enterococcus faecium* being the predominant species and vanA subtypes being the most prevalent cause of infection in hospitalized patients. Over time, the objectives of VRE prevention strategies in hospitals have moved from a focus upon containment and clearance to control and early/targeted therapies.

In this issue of ***Leukemia and Lymphoma***, Rosko *et al*. describe VRE infections in hematology patients at a single US center, spanning a 14-year period (1998–2011), comparing incidence in patients who underwent hematopoietic cell transplant (HCT) with that in non-transplanted patients [2]. During this period, VRE accounted for 14% and 10% of all bloodstream infections in HCT and non-HCT groups, respectively, consistent with endemnicity at the studied center. VRE infection rates were comparable in HCT recipients compared to non-HCT patients, and infections were predominantly due to *E. faecium*. Although 45% of patients with VRE infection died during the incident period of hospitalization, attributable mortality associated with VRE infection could not be determined from this retrospective study.

Risk factors for VRE bloodstream infection have previously been identified in hematology patients. These include antibiotic exposure (particularly to cephalosporin agents or vancomycin), prolonged hospitalization, an underlying diagnosis of acute myeloid leukemia (AML), gastrointestinal procedures and renal impairment [1,3]. Colonization has also been identified as a risk factor for subsequent bloodstream infection. Risks for development of infection and the timing of onset for infection following colonization are likely to depend upon underlying immunocompromise.

Findings of Rosko *et al*. indicate that risk factors for VRE infection are present in both transplanted and non-transplanted patient groups, and this is consistent with previous observations of these cohorts [4]. This is conceivable in an era where increasing immunosuppression in non-transplanted groups may result in more frequent healthcare contact. Some risk factors (e.g. antibiotic exposure) may be common to both groups. However, other risk factors may be unique for transplanted, non-transplanted or other subpopulations. For example, patients undergoing HCT may be managed in single-room environments with dedicated bathrooms, therefore meaning that the potential for VRE transmission is minimized. This group may have significant mucositis and therefore be predisposed to bloodstream infection following translocation of gut pathogens such as VRE. In contrast, non-transplanted patients may be located in open ward environments, and have less severe grades of mucositis, meaning that the risk of acquisition by direct transmission may be relatively higher. Even if infection rates are observed to be similar across a range of hematology subpopulations, the contributing risk factors may be quite different, and this has implications for tailoring of effectual prevention programs.

Outcomes of VRE infection have been variably reported in hematology patients. Increased healthcare costs have been ascribed to VRE bloodstream infections, where hospitalization is increased by 2.2–3.5 days [5]. Mortality at 30 days has been reported in up to 35% of VRE-infected patients [6], but this is confounded by severity of underlying disease. Molecular analysis of VRE isolates has demonstrated that adverse outcomes are not associated with increased virulence of VRE in hematology patients [7], suggesting that host factors are more relevant to infection outcomes. Indeed, poorer outcomes have been observed in the early period following allogeneic transplant [8]. Outcome data presented by Rosko *et al*. reflect the confounding influence of severity of disease and complications of therapy in patients with VRE bloodstream infection, given

Correspondence: Dr. Leon Worth, Department of Infectious Diseases and Infection Prevention, Peter MacCallum Cancer Centre, East Melbourne, Australia. Tel: + 61-03-96565853. Fax: + 61-03-96561185. E-mail: leon.worth@petermac.org

This commentary accompanies an article to be published in *Leukemia & Lymphoma*. Please refer to the table of contents of the print issue in which this commentary appears.

the high predominance of patients with underlying AML and umbilical cord blood transplant.

Targeted measures to control VRE must be applied in at-risk populations, and resources should be allocated to enable control within emergent risk groups. Risks for VRE infection must be assessed at a hospital level. If risks are deemed to be high across a broad range of patients or wards, widespread measures for control may be necessary. At minimum, active surveillance, improved hand hygiene compliance, antibiotic stewardship and hypochlorite-based environmental cleaning have traditionally been recommended [9,10]. Additional and novel approaches include hydrogen peroxide vapor for environmental decontamination [11] and chlorhexidine bathing of patients [12]. Given the fact that long-term application and sustainability of a prevention program is required for an endemic pathogen, further studies evaluating the cost-benefit of multimodal programs to control endemic VRE are required to inform rational infection prevention programs.

It is important that individual components of prevention strategies be periodically reviewed, and for sustainability and clinical benefits to be evaluated. In contrast to consensus guidelines for VRE prevention [9], donning of gloves by healthcare workers and isolation of patients have recently been demonstrated not to be essential in successful multimodal programs for control of VRE [10,13]. Specific components of prevention strategies in hematology patients have not been similarly evaluated. Future studies must differentiate between epidemic and endemic VRE, in order that customized strategies for prevention can be applied in each of these settings.

Timely commencement of targeted antibiotic therapy is necessary if VRE infection is suspected or confirmed. For hematology patients with febrile neutropenia, this requires knowledge of past colonization or infection, as well as preliminary laboratory findings (e.g. gram-positive cocci identified in a blood culture), before a decision to commence a VRE-active agent (e.g. daptomycin or linezolid) is made. This is consistent with published guidelines for the management of febrile neutropenia [14], which support empiric β-lactam monotherapy in the first instance. The emergence of endemic VRE does not justify the use of VRE-active agents as first-line empiric therapy for febrile neutropenia, unless high rates of infection have been observed in the setting of appropriate infection prevention measures. This further underscores the need for appropriately collected local longitudinal data concerning hematology patients within healthcare facilities and the value of VRE surveillance programs where VRE is endemic.

Within a healthcare facility or hospital unit, endemic VRE may be reflected by a baseline prevalence of colonization or infection, expanding populations in whom infection is detected or polyclonality of VRE isolates [9]. Despite endemnicity, a *laissez-faire* approach is not merited, as customized prevention and harm-minimization strategies continue to demonstrate an impact in reducing VRE infection in these settings [15]. This represents a challenge for infection prevention and hematology units, where longitudinal surveillance data and clinical outcomes are required to determine the scope and burden of illness in the range of treated patients. It is likely that initiatives to improve hand hygiene compliance and timely commencement of targeted antibiotics for VRE infection would be supported widely for both HCT and non-HCT hematology populations. However, the uptake and resourcing of enhanced prevention strategies for control of endemic VRE calls for longitudinal study in facilities where VRE infection is prevalent, together with cost-benefit analysis in hematology patients.

Potential conflict of interest: A disclosure form provided by the author is available with the full text of this article at www.informahealthcare.com/lal.

References

[1] Timmers GJ, van der Zwet WC, Simoons-Smit IM, et al. Outbreak of vancomycin-resistant Enterococcus faecium in a haematology unit: risk factor assessment and successful control of the epidemic. Br J Haematol 2002;116:826–833.
[2] Rosko A, Corriveau M, Suwantarat N, et al. Vancomycin-resistant enterococci infection: not just for the transplanted. Leuk Lymphoma 2014;55:1320–1325.
[3] Worth LJ, Thursky KA, Seymour JF, et al. Vancomycin-resistant Enterococcus faecium infection in patients with hematologic malignancy: patients with acute myeloid leukemia are at high-risk. Eur J Haematol 2007;79:226–233.
[4] Calderwood MS, Mauer A, Tolentino J, et al. Epidemiology of vancomycin-resistant enterococci among patients on an adult stem cell transplant unit: observations from an active surveillance program. Infect Control Hosp Epidemiol 2008;29:1019–1025.
[5] Butler AM, Olsen MA, Merz LR, et al. Attributable costs of enterococcal bloodstream infections in a nonsurgical hospital cohort. Infect Control Hosp Epidemiol 2010;31:28–35.
[6] Weinstock DM, Conlon M, Iovino C, et al. Colonization, bloodstream infection, and mortality caused by vancomycin-resistant enterococcus early after allogeneic hematopoietic stem cell transplant. Biol Blood Marrow Transplant 2007;13:615–621.
[7] Worth LJ, Slavin MA, Vankerckhoven V, et al. Virulence determinants in vancomycin-resistant Enterococcus faecium vanB: clonal distribution, prevalence and significance of esp and hyl in Australian patients with haematological disorders. J Hosp Infect 2008;68:137–144.
[8] Kamboj M, Chung D, Seo SK, et al. The changing epidemiology of vancomycin-resistant Enterococcus (VRE) bacteremia in allogeneic hematopoietic stem cell transplant (HSCT) recipients. Biol Blood Marrow Transplant 2010;16:1576–1581.
[9] Muto CA, Jernigan JA, Ostrowsky BE, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of Staphylococcus aureus and enterococcus. Infect Control Hosp Epidemiol 2003;24:362–386.
[10] Grabsch EA, Mahony AA, Cameron DR, et al. Significant reduction in vancomycin-resistant enterococcus colonization and bacteraemia after introduction of a bleach-based cleaning-disinfection programme. J Hosp Infect 2012;82:234–242.
[11] Passaretti CL, Otter JA, Reich NG, et al. An evaluation of environmental decontamination with hydrogen peroxide vapor for reducing the risk of patient acquisition of multidrug-resistant organisms. Clin Infect Dis 2013;56:27–35.
[12] Kassakian SZ, Mermel LA, Jefferson JA, et al. Impact of chlorhexidine bathing on hospital-acquired infections among general medical patients. Infect Control Hosp Epidemiol 2011;32:238–243.
[13] Tschudin Sutter S, Frei R, Dangel M, et al. Not all patients with vancomycin-resistant enterococci need to be isolated. Clin Infect Dis 2010;51:678–683.
[14] Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. Clin Infect Dis 2011;52:e56–e93.
[15] Morris-Downes M, Smyth EG, Moore J, et al. Surveillance and endemic vancomycin-resistant enterococci: some success in control is possible. J Hosp Infect 2010;75:228–233.