American Journal of Infection Control 44 (2016) 515-9

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Impact of vancomycin-resistant enterococci colonization in critically ill pediatric patients

Murat Sutcu MD [a], Hacer Akturk MD [a,*], Manolya Acar MD [a], Nuran Salman MD [a], Derya Aydın MD [b], Bahar Akgun Karapınar MD [b], Aslı Ozdemir RN [c], Rukiye Cihan RN [c], Agop Citak MD [d], Ayper Somer MD [a]

[a] Department of Pediatric Infectious Diseases, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey
[b] Department of Clinical Microbiology, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey
[c] Hospital Infection Control Committee, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey
[d] Department of Pediatric Intensive Care, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey

Key Words:
Vancomycin-resistant enterococci
colonization
infection
pediatric intensive care unit

Background: We aimed to determine the frequency of vancomycin-resistant enterococci (VRE) infection occurrence in previously VRE-colonized children in a pediatric intensive care unit (PICU) and to identify associated risk factors.

Methods: Infection control nurses have performed prospective surveillance of health care–associated infections and rectal VRE carriage in PICUs from January 2010-December 2014. This database was reviewed to obtain information about VRE-colonized and subsequently infected patients. A case-control study was performed to identify risk factors associated with VRE infection development in previously VRE-colonized patients.

Results: Out of 1,134 patients admitted to the PICU, 108 (9.5%) were found to be colonized with VRE throughout the study period. Systemic VRE infections developed in 11 VRE-colonized patients (10.2%), and these included primary bloodstream infection (n = 6), urinary tract infection (n = 3), meningitis and bloodstream infection (n = 1), and meningitis (n = 1). Logistic regression analysis indicated long hospital stay (≥30 days) and glycopeptide use after detection of VRE colonization as risk factors for developing VRE infection in VRE-colonized patients (odds ratio [OR], 5.76; 95% confidence interval [CI], 1.6-15.8; $P = .017$ and OR, 12.8; 95% CI, 1.9-26.6; $P = .012$, respectively).

Conclusions: VRE colonization has important consequences in pediatric critically ill patients. Strict infection control measures should be implemented to prevent VRE colonization and thereby VRE infections. Furthermore, irrational antibiotic use and particularly glycopeptide use in VRE-colonized patients should be restricted.

Enterococcus spp are members of the normal human flora, especially of the gastrointestinal tract. Acquisition of resistance to glycopeptide antibiotics (ie, vancomycin, teicoplanin) was first identified in 1988.[1] Since then, *Enterococcus* spp resistant to glycopeptide antibiotics, vancomycin-resistant enterococci (VRE), has become one of the important causative agents of health care–associated infections (HCAIs), with variations across time and institutions. Recently published data from the United States indicated enterococci (14% of 69,475 HCAIs) as the second most frequent cause of HCAIs and VRE (3%) as the second most frequent cause of multidrug-resistant HCAIs after methicillin-resistant *Staphylococcus aureus*.[2] A recent European survey including >230,000 patients reported enterococci as the third most common cause of HCAIs, of which 10% were VRE.[3]

Critically ill patients are at higher risk of being colonized with VRE because of severe underlying illnesses, high rate of invasive procedures, use of multiple broad-spectrum antibiotics, and longer stay of hospital.[4-6] Hence, many hospitals prefer to implement surveillance of VRE rectal colonization in high-risk wards such as intensive care units. Active VRE surveillance together with other precautionary measures can control VRE colonization,[7] which is the primary risk for subsequent occurrence of VRE infection.[4,8-10] However, what other factors contribute to the development of a systemic VRE

* Address correspondence to Hacer Akturk, MD, Tophanelioğlu cad. Güzelyapı Sitesi A Blok D:12 Altunizade, Üsküdar, Istanbul, Turkey.
E-mail address: hacergunakturk@gmail.com (H. Akturk).
Conflicts of Interest: None to report.

0196-6553/
http://dx.doi.org/10.1016/j.ajic.2015.11.026

infection in a patient rectally colonized with VRE is a rarely investigated issue, especially in pediatric critically ill patients. Therefore, this study was planned to determine the frequency of VRE infection development in VRE-colonized patients admitted to a pediatric intensive care unit (PICU) over a 5-year period and to evaluate risk factors for progression to infection.

METHODS

Hospital setting

This study was conducted in the PICU of a tertiary referral university hospital. It is a 6-bed intensive care unit accepting complicated pediatric patients aged 1 month to 18 years old. It has 2 rooms with 3 patient beds within each. No isolation room exists in the PICU. The patient to nurse ratio is 2:1.

Study design, patients, and data collection

A retrospective case-control study was conducted involving a 5-year period from January 2010-December 2014. Since January 2010, active surveillance of VRE rectal colonization has been performed in selective high-risk wards of our institution, including the PICU. Rectal swabs of patients admitted to the PICU are routinely screened for presence of VRE within 48-72 hours of admission and once a week thereafter. When a patient is detected to be positive, strict contact precautions are used mainly because no isolation rooms exist in the PICU.

Infection control nurses assigned from the Hospital Infection Control Committee prospectively tracked all HCAIs occurring in patients admitted to the PICU together with the results of rectal VRE surveillance and reported to the Hospital Infection Control Committee monthly. They determined whether VRE isolated from clinical specimens represented an infection or colonization based on definitions from the Centers for Disease Control and Prevention.[11] This database was used to determine pediatric patients rectally colonized with VRE and the subgroup of colonized patients who developed subsequent systemic VRE infection. The medical records of the patients identified as colonized or infected with VRE were also reviewed to reveal detailed clinical characteristics. A case-control study was performed and VRE-colonized patients who developed subsequent systemic VRE infection (cases; VRE-I) were compared with VRE-colonized patients who did not developed systemic VRE infection (controls; VRE-C) regarding possible risk factors.

Definitions

VRE colonization was defined as a positive rectal swab taken as part of routine surveillance in a patient in the absence of any clinical specimens yielding VRE. Systemic VRE infection was defined as isolation of VRE from a clinical specimen together with signs and symptoms of infection in a patient previously colonized with VRE. Types of HCAIs were defined according to Centers for Disease Control and Prevention–based definitions.[11]

Patients with known VRE colonization prior to admission or found to be positive in the first 48-72 hours of admission were defined as imported cases. On the other hand, the term cross-transmission was used for the patients who had negative rectal swabs in the first 72 hours of admission and who acquired VRE colonization during the current admission to the PICU. Undetermined cases were those who could not be sampled in the first 72 hours of admission.

Microbiologic procedures

Rectal swab samples were collected on sterile transport medium (Copan). They were inoculated onto bile esculin azide agar (Enterococcosel™ Agar; BD, Heidelberg, Germany) containing 6 μg/mL of vancomycin and tryptic soy broth (Tryptone Soya Broth [U.S.P.]; Oxoid, Hampshire, UK), including sodium azide (Tryptone Soya Broth [U.S.P.]; Sigma-Aldrich, Shanghai, China).[12] Incubation was performed at 35°C-37°C in normal atmosphere. After 24 hours, agar plates were checked for the presence of black-colored colonies caused by esculin hydrolysis. A vancomycin susceptibility test was performed by the disk diffusion method according to the Clinical and Laboratory Standards Institute.[13] If vancomycin resistance was determined, then a pyrrolidonyl arylamidase (BBL DrySlide PYR Kit; BD) test was performed to confirm the species as *Enterococcus*. After 24 hours, the bacteria which had grown in the sodium azide broth were subcultured to bile esculin azide agar, and the procedure previously described was repeated. Blood samples were cultured in a BACTEC 9120 Blood Culture System (BD). Positive blood cultures were subcultured onto 5% sheep blood agar (BD) and chocolate agar (BD) and incubated at 35°C-37°C in 5% CO_2 atmosphere. Urine samples were inoculated onto chromogenic agar (chromID; bioMérieux, Marcy-l'Étoile, France) and incubated at 35°C-37°C in normal atmosphere. Cerebrospinal fluid samples were inoculated onto 5% sheep blood agar and chocolate agar and incubated at 35°C-37°C in 5% CO_2 atmosphere. All samples were incubated for 48 hours. Identification was performed by classical methods, including gram stain, catalase test, esculin hydrolysis, pyrrolidonyl arylamidase test, or automatic identification system (VITEK 2; bioMérieux). Vancomycin and teicoplanin mean inhibitory concentrations were determined by epsilometer test (Etest; bioMérieux), and the results were evaluated according to the Clinical and Laboratory Standards Institute standards.[13]

Statistics

All statistical analyses were performed with SPSS for Windows version 21.0 (SPSS, Chicago, IL). Normality was assessed by Shapiro-Wilk tests and histogram graphics. Data are presented as median, minimum, maximum, frequency, and percentage. Categorical variables between groups were compared with the χ^2 test or Fisher exact test when the expected cell size was <5. Normally distributed continuous variables were compared by Student *t* test. Mann-Whitney *U* test was used for continuous variables, which are not normally distributed. All *P* values are based on 2-tailed statistical analyses, and $P < .05$ was considered statistically significant. The significant predictors of VRE infection with $P \leq .10$ in univariate analysis were fitted to perform a logistic regression analysis model to identify independent risk factors associated with VRE infection occurrence.

RESULTS

Between January 2010 and December 2014, 1,134 patients were admitted to the PICU of our institution. One hundred and eight patients (9.5%) were found to be colonized with VRE throughout the study period. Species determination could be performed in rectal samples of 40 patients: *E faecium* in 36 patients, *E gallinarum* in 3 patients, and nontypeable *Enterococcus* in 1 patient. Twenty-five patients (23%) were colonized with VRE on admission (imported cases), and 82 patients (75%) acquired VRE colonization during their PICU stay (cross-transmission). Only 1 patient was an undetermined case. Only 5 patients were known to be already colonized with VRE on admission to the PICU. Others were designated as imported cases because of their positive rectal swabs in the first 48-72 hours of PICU admission. VRE-colonized patients were admitted to the PICU from