Vancomycin resistant enterococci colonization in a neonatal intensive care unit: case-control study

Yenidoğan yoğun bakım ünitesi'nde vankomisin dirençli enterokok kolonizasyonu: vaka-kontrol çalışması

Vancomycin resistant enterococci in neonates

Bilge Tanyeri-Bayraktar[1], Süleyman Bayraktar[2]
[1]Department of Neonatology, Bezmialem Vakif University,
[2]Pediatric Intensive Care Unit, Haseki Training and Research Hospital, İstanbul, Turkey

Öz

Amaç: Vankomisin dirençli enterok (VDE), hastane kaynaklı ve yoğun bakım hastalarıyla ilişkili bir mikroorganizmadır. Bu çalışmanın amacı, yenidoğan yoğun bakım ünitesinde, VDE kolonizasyonuna etki eden risk faktörlerini, salgını kontrol etmeye yönelik önlemleri ve VDE kolonizasyonunda Lactobacillus reuteri'nin etkisini incelemektir. Gereç ve Yöntem: Çalışma Aralık 2012-Haziran 2013 arasında 39 vaka ve 78 kontrol ile yapılan bir vaka-kontrol çalışmasıydı. Çalışmada birincil olarak, VDE kolonizasyonuna etki eden risk faktörlerinin belirlenmesi hedeflendi. İkincil amaç da VDE eliminasyonunda Lactobacillus reuteri'nin etkisini belirlemekti. Bulgular: İkiyüz yetmiş iki yenidoğanın 39'u (%14.3) VDE ile kolonize idi. Çok değişkenli analizlere göre VDE kolonizasyonu için risk faktörleri gebelik yaşı, ortak ultrasonografi kullanımı ve metisilin dirençli antistafilokokal antibiotik kullanımı olarak bulunmuştur. VDE pozitif olan hastaların 26'sı Lactobacillus reuteri aldı. 26 hastanın 11'i (%42.3) probiyotik kullanımından sonra negatifleşti. VDE'nin negatifleşme süresi 9.61 ± 5.53 gün idi. Tartışma: Vankomisin dirençli enterokok kolonizasyonunda, düşük gebelik haftası, ultrasonografi cihazının ortak kullanılması ve metisilin dirençli antistafilokokal ilaç kullanımı bağımsız risk faktörleri idi. Ünite içinde yayılımı engellemek için etkin enfeksiyon kontrol programı uygulanmalıdır. VDE kolonizasyonunda probiotiklerin etkinliğini belirlemek için ise ileri randomize kontrollü çalışmalara ihtiyaç vardır.

Anahtar Kelimeler

Vankomisin Dirençli Enterokok; Yenidoğan; Laktobasillus Reuteri; Probiyotik

Abstract

Aim: Vancomycin-resistant enterococcus (VRE) is a concerning microorganism among hospitalized and intensive care patients. The aim of this study was to report the outbreak characteristics, the risk factors, and the outbreak control of VRE colonization in a neonatal intensive care unit and the effect of Lactobacillus reuteri on VRE colonization. Material and Method: Thirty- nine cases and seventy-eight controls were included in the case-control study between December 2012- June 2013. The primary outcome variable was the risk factors of VRE colonization. The secondary outcome was the effect of Lactobacillus reuteri on elimination of VRE. Results: Of 272 neonates, 39 (14.3%) were colonized with VRE. Multivariate analysis suggested that gestational age, shared use of ultrasonography, and receiving anti-methicillin resistant staphylococcus aureus drugs were the risk factors of VRE colonization. Twenty-six of the 39 VRE positive patients received Lactobacillus reuteri. Eleven (42.3%) of 26 patients became negative after the use of probiotics. The clearance time of VRE was 9.61 ± 5.53 days. Discussion: Low gestational age, shared ultrasonography, and anti- methicillin resistant staphylococcus aureus drug exposure are major independent risk factors for VRE colonization. An effective infection control programme should be implemented. To determine the effectiveness of probiotics in VRE colonization, further randomized controlled trials must be conducted.

Keywords

Vancomycin-Resistant Enterococci; Neonate; Lactobacillus Reuteri; Probiotic

DOI: 10.4328/JCAM.4989 Received: 22.03.2017 Accepted: 12.05.2017 Printed: 01.12.2017 J Clin Anal Med 2017;8(suppl 4): 276-9
Corresponding Author: Süleyman Bayraktar, Pediatric Intensive Care Unit, Haseki Training and Research Hospital, 34250, Fatih, Istanbul, Turkey.
GSM: +905323851078 F.: +90 2125896229 E-Mail: bsuleyman@hotmail.com

Introduction

Vancomycin-resistant enterococcus (VRE) is a concerning microorganism among hospitalized and intensive care patients. The US Centers for Disease Control and Prevention reported VRE as having a 28.5% prevalence rate in intensive care units [1]. Morbidity, mortality, and hospital costs are increased due to VRE infections. The patients who are exposed to healthcare settings have an increased risk of VRE. It is already known that VRE transmission occurs primarily by ward staff members [2].

There have been inadequate studies about outbreaks of VRE in neonatal intensive care units (NICU). We described here outbreak characteristics, the risk factors for VRE colonization, and the outbreak control of VRE colonization in the NICU. We also evaluated the effect of Lactobacillus reuteri (L.reuteri) to eliminate the VRE colonization.

Material and Method

This was a retrospective, case-control study of VRE colonization at a university hospital in Istanbul, Turkey, a referral hospital providing tertiary care in NICU. Approximately 500 patients are admitted to the NICU annually.

Population

Records were obtained from the database of NICU patients for December 2012 through June 2013. The surveillance for VRE in NICU was started in December 2012 after the detection of the first patient colonized with VRE in urine culture.

Case definition

The index case was admitted from the emergency room and was born in a private hospital. He was 12 days old on admission and hospitalized for insufficient breastfeeding. He had also the phenotype of Down syndrome. VRE was detected in the urine culture which was taken on admission. Subsequently VRE surveillance was started by the Infection Control Section in the NICU. Rectal swabs were obtained from every baby on admission to the NICU and every Monday during the hospitalization period.

Case-control study

Based on the finding of the first VRE colonized case, a case-control study was initiated. Thirty-nine patients who had VRE colonization were enrolled into the study. Seventy-eight controls were randomly matched 1:2 from the NICU admission list during the same surveillance time. The controls consisted of patients whose rectal swabs were negative of VRE.

This study had two steps. First, we evaluated the risk factors of VRE colonization and second, we explored the effect of L. reuteri on elimination of VRE. The patients received L. reuteri after informed consent was obtained from the parents. We wanted to give a probiotic (L. reuteri) to all babies who were colonized with VRE but some parents refused the use of L. reuteri. Therefore, 26 of 39 patients received L. reuteri with a dose of 5 drops/day (108 cfu) after the detection of VRE until a negative result was seen.

During the study period, surface cultures from the incubators, infusion pumps, ventilators, and computer keyboards were obtained but we could not detect VRE in the environmental spaces.

Outbreak control measures

We have revised the methods of infection control as follows:

a. The staff were re-educated on hand hygiene.

b. The nursing staff were assigned to different nurse groups according to the babies who were VRE negative and VRE positive.

c. The babies who had VRE positive swabs were housed in the same room (isolation precaution).

d. All the staff who took care of these babies used gloves and gowns.

e. Extensive cleaning of the environmental surfaces was done throughout the outbreak with Minudes (Ecolab GmbH &Co. OHG) and Cavicide TM.

f. The rounds started from the babies whose swabs were negative of VRE.

g. Shared medical equipment was disinfected before being brought into the NICU.

h. Plastic bags were used to cover the ultrasonography (USG) probes.

i. Each incubator had its own equipment, such as a stethoscope and hand disinfectant.

Microbiology

Rectal swabs for VRE cultures were first inoculated onto 5% sheep-blood agar and VRE chrome agar (Salubris, Inc., Istanbul, Turkey) for 18-24 hours. Following 24 hours of incubation, a definite spot of growth or more than one colony indicates that the Enterococci may be a VRE. The catalase test was used and if the sample was catalase negative, L-pyrolidonyl beta naphthylamid (PYR) was done. Identification (E. faecalis/ E. faecium) was confirmed by the Vitek®2 (Biomeriux, France) fully automated microbiological system. Susceptibility testing was done by the same system.

Statistical analysis

Data were entered into a database using SPSS 10.0 for Windows (SPSS Inc, Chicago, USA). The X2 test and the independent samples t-test were used for categorical and continuous variables, respectively. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated. A stepwise multivariate logistic regression was conducted to examine the association of risk factors controlling potential confounders. The logistic model included all variables for which a p value of <0.05 was obtained in the multivariate analysis. A p value of <0.05 was considered significant.

Results: In a retrospective approach, 272 neonates were identified in the surveillance population, of whom 39 (14.3%) were colonized with VRE. The duration of VRE colonization was 14.5±24.69 (min 0-max 150) days.

The main epidemiological characteristics of cases and controls are shown in Table 1. The mean gestational ages and weights of cases were lower than in the controls (p<0.001).

Multivariate analysis suggested that gestational age, use of shared USG, and receiving anti-methicillin-resistant staphylococcus aureus (MRSA) drugs (vancomycin-teicoplanin) were the risk factors of VRE colonization in the NICU (Table 2).

Twenty-six of the 39 VRE positive patients received L. reuteri. Eleven (42.3%) of 26 patients became negative after the use of probiotics. The clearance time of VRE was 9.61 ± 5.53 (min

5-max 26) days. Only two (15.4%) of 13 patients who did not receive L. reuteri had clearance of VRE. There was no VRE infection during the surveillance period. All VRE were identified as E. faecium. Molecular tests could not be done to show the clonal relationship due to financial difficulties.

Table 1. Characteristics of case and control patients

Feature	Cases (n=39)	Controls (n=78)	p value
Sex, male	24	51	0.68
Gestational age, weeks, mean±SD	34.18±3.82	37.65±2.02	<0.001
Gestational weight, g, mean±SD Range, g	2172.18±891.97 (510-3900)	3057.77±672.22 (1840-4440)	0.0001
Born in study hospital	35	59	0.07
Delivery mode, C/S	29	43	0.04
Respiratory distress, Mechanical ventilation	17	6	0.0001
TPN, duration, days (median)	14.42±9.70	4.92±3.20	0.002
Nasogastric tube,n	22	11	0.0001
USG, n	34	28	0.0001
Central lines (CVC, UVC)	12	6	0.002
Antimicrobial agents			
Vancomycin,n	10	0	0.0001
Teicoplanin,n	5	1	0.008
Meropenem,n	17	3	0.0001
Ampicillin,n	24	29	0.01
Duration of hospitalization	27.02±30.51	5.42±4.18	0.0001

p<0. 05 is statistically significant

Table 2. Multivariate odds ratios of potential risk factors for VRE colonization

Risk factors	OR (95%CI)	p
Gestational age	0.78 (0.62-0.97)	0.027
Anti-MRSA drug	9.17 (1.01=83.06)	0.049
USG	4.43 (1.35-14.47)	0.014

p<0.05 is statistically significant

Subtitles:
C/S: Cesarean section
CVC: Central venous catheter
MRSA: Methicillin-resistant staphylococcus aureus
USG: Ultrasonography
UVC: Umbilical venous catheter
TPN: Total parenteral nutrition
VRE: Vancomycin- resistant enterococcus

Discussion

Our study demonstrated that gestational age, anti-MRSA drug exposure, and the use of shared USG are major independent risk factors for VRE colonization. We could not determine the effect of L. reuteri on clearance of VRE statistically, but the clearance was much higher in babies who received L. reuteri. The colonization rate of VRE was 14.3% in our NICU during the seven month period. The data about the colonization rate of VRE in NICUs in Turkey is limited. A study by Akturk et al. reported it as 12% [3].

Intrahospital transfer, hemodialysis, receiving antimicrobial drugs, and malignancies have been reported as risk factors for VRE colonization. Low birth weight was previously reported as a risk factor for VRE colonization in the literature [1-4-5-6]. Tapering off vancomycin use was also mentioned as an important factor to keep an outbreak of VRE under control. Prior use of antimicrobial therapy, including vancomycin and cephalosporin, has been shown to be associated with acquisition of VRE [5-7-8)]. In a study by Askarian et al. [7], this factor was also significant and increased the risk for VRE colonization 3-fold.

It was reported that VRE colonization is more frequently seen in units where patients were hospitalized longer [3-5-9]. It is also seen more frequently in neonates requiring prolonged mechanical ventilation, use of vascular catheters, prolonged total parenteral nutrition, prolonged duration of hospitalization, and frequent exposure to antibiotics, especially anti-MRSA [3]. Askarian et al. [7], mentioned that all VRE positive patients were VRE negative on admission and 80% of these patients were colonized early in the first week of hospitalization.

Shared personnel and/or medical equipment may be responsible for the transmission of VRE [10]. It has been reported that ultrasound nebulizer use increased VRE colonization [11]. Rapid spread of VRE can be seen among neonates in NICUs [10]. Staff should be further educated to improve standard precautions and contact precautions and the appropriate selection of antibiotics should be promoted to avoid the spread of VRE in the hospital environment [5-8-10-11]. Strict infection control measures can decrease the rate of VRE colonization among neonates.

Therapeutic options for VRE infections are limited. Oral bacitracin with or without gentamycin was ineffective for the clearance of VRE [12]. It is important to consider that colonized babies have a large occult reservoir for transmission of VRE [3-13]. Surveillance studies could prevent the development of such a reservoir. In many reports it was mentioned that contact isolation, cohorting of patients, and strict and proper decontamination of surfaces may control the transmission of VRE [3-12-14].

Probiotics are the agents that have been used in several studies to improve the intestinal microbial balance [15]. There is no conclusive evidence about the effect of probiotics in eradicating or preventing VRE. There are few studies in which probiotics were used in VRE colonized patients; also, the proper dose of probiotics has not been researched in any study [16]. In our study, the sample is small so the statistical analysis is not significant. To evaluate the effectiveness of L. reuteri in elimination of VRE, large, prospective studies are needed. Also, the effective dose of probiotics should be investigated.

The present study has some limitations. First, it is a retrospective study; however, we matched the patients well according to the surveillance period. Second, the number of cases who received L. reuteri was small. If the number of cases had been higher, a significant effect of L. reuteri treatment may have been determined. Third, while the study was retrospective we could not research the effective dose of L. reuteri due to infant's weight or use of antibiotics.

There is an urgent need to restrict the unjustified use of anti-MRSA drugs as much as possible. Just as important, transmission of VRE is the best indicator for measuring the compliance with hand hygiene protocols and also for decontamination of environment. We have to evaluate the most effective infection control programs for stopping the spread of VRE in the NICU and the hospital.

Acknowledgements

We thank Monica Ann Malt for English editing.

Competing interests

The authors declare that they have no competing interests.

References

1. Hufnagel M, Liese C, Loescher C, Kunze M, Proempeler H, Berner R, et al. Enterococcal colonization of infants in a neonatal intensive care unit: associated predictors, risk factors and seasonal patterns. BMC Infect Dis 2007;16 (7):107.
2. Pusch T, Kemp D, Trevino S, Button T, Sanchez P, Gander R, et al. Controlling outbreak of vancomycin-resistant Enterococcus faecium among infants caused by an endemic strain in adult inpatients. Am J Infect Control 2013;41 (1):51-6.
3. Akturk H, Sutcu M, Somer A, Acar M, Karapınar BA, Aydin D, et al. Vancomycin-resistant enterococci colonization in a neonatal intensive care unit: who will be infected? J Matern Fetal Neonatal Med 2016;29(21):3478-82.
4. Sherer CR, Sprague BM, Campos JM, Nambiar S, Temple R, Short B, et al. Characterizing vancomycin-resistant enterococci in neonatal intensive care. Emerg Infect Dis 2005;11(9):1470-2.
5. Ulu-Kilic A, Özhan E, Altun D, Perçin D, Güneş T, Alp E. Is it worth screening for vancomycin-resistant Enterococcus faecium colonization?: Financial burden of screening in a developing country. AJIC 2016;44:e45-e49.
6. Kara A, Devrim İ, Bayram N, Katipoğlu N, Kıran E, Oruç Y, et al. Risk of vancomycin-resistant enterococci bloodstream infection among patients colonized with vancomycin-resistant enterococci. Braz J Infect Dis 2015;19(1):58-61.
7. Askarian M, Afkhamzadeh R, Monabbati A, Daxboeck F, Assadian O. Risk factors for rectal colonization with vancomycin-resistant enterococci in Shiraz, Iran. Int J Infect Dis 2008;12 (2):171-5.
8. Shorman M, Al-Tawfiq JA. Risk factors associated with vancomycin-resistant Enterococcus in intensive care unit settings in Saudi Arabia. Interdiscip Perspect Infect Dis 2013;2013:369674.
9. Bizzarro MJ, Gallagher PG. Antibiotic-Resistant organisms in the neonatal intensive care unit. Semin Perinatol 2007;31 (1):26-32.
10. Malik RK, Montecalvo MA, Reale MR, Li K, Maw M, Munoz JL et al. Epidemiology and control of vancomycin-resistant enterococci in a regional neonatal intensive care unit. Pediatr Infect Dis J 1999; 18(4):352-6.
11. Hoshuyama T, Moriguchi H, Muratani T, Matsumoto T. Vancomycin- resistant enterococci (VRE) outbreak at a university hospital in Kitakyushu, Japan: case-control studies. J Infect Chemother 2008; 14 (5):354-60.
12. Ergaz Z, Arad I, Bar-Oz B, Peleg O, Benenson S, Minster N, et al. Elimination of vancomycin-resistant enterococci from a neonatal intensive care unit following an outbreak. J Hosp Infect 2010;74:370-6.
13. Duchon J, Graham III P, Della-Latta P, Whittier S, Carp D, Bateman D, et al. Epidemiology of enterococci in a neonatal intensive care unit. Infect Control Hosp Epidemiol 2008;29 (4):374-6.
14. Ergani-Ozcan A, Naas T, Baysan BO, Ogunc D, Inan D, Colak D, et al. Nosocomial outbreak of vancomycin-resistant Enterococcus faecium in a paediatric unit at a Turkish university hospital. J Antimicrob Chemother 2008;61:1033-9.
15. Vidal M, Forestier C, Charbonnel N, Henard S, Rabaud C, Lesens O. Probiotics and intestinal colonization by vancomycin-resistant enterococci in mice and humans. J Clin Microbiol 2010; 48(7):2595-8.
16. Manley KJ, Fraenkel MB, Mayall BC, Power DA. Probiotic treatment of vancomycin-resistant enterococci: a randomized controlled trial. Med J Aust 2007;186 (9):454-7.

How to cite this article:

Bayraktar BT, Bayraktar S. Vancomycin Resistant Enterococci Colonization in a Neonatal Intensive Care Unit: Case-Control Study. J Clin Anal Med 2017;8(suppl 4): 276-9.