Turkish Journal of Medical Sciences

Volume 40 | Number 4 Article 17

1-1-2010

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TÜBİTAK

Original Article

Turk J Med Sci
2010; 40 (4): 623-628
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E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-0810-2

Absence of vancomycin-resistant enterococci (VRE) despite the presence of risk factors: a survey of rectal carriage of VRE*

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Aim: The resistant organisms from patients and healthcare workers (HCWs) first colonized the gastrointestinal tract before causing infections in patients. In this study, presence of risk factors for vancomycin-resistant enterococci (VRE) colonization and the prevalence of rectal carriage of VRE among HCWs and hospitalized patients in the absence of an outbreak were investigated. Design: Cross-sectional study. Setting: A 600-bed training and research hospital.

Materials and methods: A total of 508 intensive-care unit (ICU) patients and HCWs in these units were included. Risk factors such as previous antibiotic use, especially vancomycin and cephalosporin, the presence of invasive devices like catheters, and co-morbid diseases were investigated. Rectal smear cultures were obtained from each participant to detect VRE colonization.

Results: Risk factors for VRE colonization were identified among both patients and HCWs with a significant ratio. Except for one patient, who had been transferred from another hospital, no VRE colonization was detected in patients or HCWs.

Conclusion: The result was attributed to factors such as low inter-institutional transfer, HCWs' being free of VRE colonization (transmission is less likely), strict infection control strategy of the hospital, isolation of newly transferred patients suspected of having VRE colonization, isolation of VRE colonization identified patients, use of indwelling catheters only when indicated and their early removal, and low prevalence of predisposing co-morbid diseases and malignity. We want to underline that a strict hospital infection control program can prevent colonization, even in the presence of risk factors.

Key words: VRE, VRE colonization, nosocomial surveillance

Risk faktörlerinin bulunmasına rağmen vankomisin dirençli enterokokun (VRE) bulunmaması: bir VRE rektal taşıyıcılık surveyansı

Amaç: Dirençli mikororganizmalar, hastalığa sebep olmadan önce, hastaların ve sağlık çalışanlarının ilk olarak gastrointestinal sisteminde kolonize olurlar. Bu çalışmada hastanede yatan hastalarda ve sağlık çalışanlarında vankomisine dirençli enterokok (VRE) kolonizasyonu ve taşıyıcılık için risk faktörlerinin bulunup bulunmadığının araştırılması amaçlanmıştır.

Yöntem ve gereç: Çalışma 600 yataklı bir eğitim ve araştırma hastanesinde yapıldı. Özellikle yoğun bakımda yatan hastalar olmak üzere 508 yataklı hasta ve sağlık çalışanı çalışmaya dahil edildi. Antibiyotik kullanım geçmişi, katater varlığı, eşlik eden hastalık varlığı gibi risk faktörleri sorgulandı. VRE kolonizasyonu araştırılmak üzere rektal sürüntü kültürleri alındı.

Bulgular: Hem hasta grubunda hem de sağlık çalışanlarında VRE kolonizasyonu için daha önceki çalışmalarda belirtilmiş olan risk faktörleri yüksek oranda saptandı. VRE kolonizasyonu başka bir hastaneden transfer edilen bir hasta hariç saptanmadı.

Received: 09.10.2008 – Accepted: 04.02.2010

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* This project was supported by the Scientific and Technological Research Council of Turkey (TÜBİTAK) with project number SBAG-AYD 493.

Sonuç: Risk faktörlerinin varlığına rağmen kolonizasyonun olmaması: hastane içi transferin az olması, sağlık çalışanlarında sıkı tarama yapılması ve VRE bulunmayışı (hastalara geçiş ihtimali daha az olacaktır), sıkı takip edilen enfeksiyon kontrol stratejisi, VRE kolonizasyonu olan hastaların izole edilmesi, damar içi kataterlerin endikasyonsuz kullanılmaması ve erken çekilmesine, malignite ve eşlik eden hastalık varlığının az olmasına bağlandı.

Anahtar sözcükler: VRE, VRE kolonizasyonu, nozokomiyal enfeksiyonlar

Introduction

The gastrointestinal tract is the main habitat of Enterococcus spp., but they are occasionally found in oropharyngeal secretions, vaginal secretions, and on the skin, especially in the perineal area. They can cause endocarditis, urinary tract infections, intra-abdominal pelvic and wound infections, peritonitis, nosocomial bacteremia, central nervous system infections, osteomyelitis, neonatal sepsis, and pneumonia (1,2). *Enterococcus faecalis* and *Enterococcus faecium* are 2 major predominant Enterococcus spp. *E. faecalis* accounted for 80% to 90% of the organisms encountered in the clinical microbiology laboratory while *E. faecium* accounted for 5% to 10% of all isolates (2).

Enterococci have the ability to improve resistance to several antibiotics easily by plasmid or transpozons. Vancomycin-resistant enterococci (VRE) are among the feared multiresistant pathogens. Like other nosocomial pathogens, they can spread within and even among hospitals (3). The high ratio of antibiotic resistance allows the bacteria to survive in the hospital environment and colonize the tracts of healthcare workers (HCWs). The problem was detected in the late 1980s, and, by 2000, 28% of ICU-acquired enterococcal infections were caused by resistant strains. In the USA, VRE are a typical hospital generated problem pathogen, while in Europe the situation is quite different; there is a high prevalence of stool carriage of VRE in the healthy community who has no previous contact with the healthcare system (4). Enterococci strains causing nosocomial infections have been occasionally found on the hands of medical personnel and have frequently been isolated from environmental sources in hospitals and nursing homes. Besides this, patients in nursing homes have been shown to be a significant reservoir of stool carriage of VRE. It also appears that resistant organisms from patients or hospital personnel first colonized the gastrointestinal tract before causing infections in patients. There is evidence that hospital personnel harboring resistant enterococci in their own gastrointestinal tracts may be responsible for colonization of patients under their care (2).

Surveillance of nosocomial infections and certain pathogens like VRE is an important hospital infection control activity. In this study we aimed to investigate the presence of risk factors for colonization with VRE and the prevalence of rectal VRE carriage in hospitalized patients and HCWs in our hospital.

Methods and subjects

Sample and setting

The study was conducted in a 600-bed government hospital (Ankara Training and Research Hospital) between August and December 2005.

Since certain departments deal more with critical patients especially with open wounds, we intended to include particularly ICUs (surgical, neurosurgical and neurology ICU, and coronary care unit) and surgical departments like general surgery, operating rooms, ear-nose-throat (ENT), orthopedics, plastic and reconstructive surgery (PRS), ophthalmology, urology, and obstetrics and gynecology. Especially the auxiliary personnel may play a role in the transmission of the bacteria; therefore, those who worked in the departments mentioned above were also included in the study. Although some hospital staffs like the catering staff are not usually in direct touch with the patients' management, we included them as well because they may play a role in the fecal oral transmission.

Procedures

The local ethical committee approval of Ankara Research and Training Hospital was obtained for the study and informed consents were signed by each HCW as well as by patients or their relatives. The stool samples from HCWs and patients were taken by

sterile rectal swabs (Cultiplast swab, L111598, 12 × 150 mm), either with the help of medical staff or, if they were capable, by themselves.

Microbiological protocols

Enterococci were identified through conventional methods (1). The rectal smears were inoculated into enterococcosel agar with ceftazidime and vancomycin (Becton, Dickinson Company, USA). Growth medium was confirmed with standard VRE strain (VRE ATCC 19433 and VRE ATCC 49474). After incubation for 24-72 h at 35 °C, the black-color-forming colonies were gram stained, catalase activity was checked, and then inoculated to bile-esculine azide agar and other media that included 6.5% sodium chloride. Vancomycin resistance was confirmed in blood agar by disc diffusion.

Data analysis

SPSS 13.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Chi-square test was used to compare categorical variables between the groups. $P < 0.05$ was accepted as statistically significant.

Results

A total of 508 subjects, 221 HCWs and 287 hospitalized patients from different clinics, were included in the study. Of the 221 HCWs, 92 (41.6%) were female and 129 (58.4%) were male, while of the 287 hospitalized patients, 136 (47.4%) were female and 151 (52.6%) were male. Mean ages of the patients and HCWs were 50.6 ± 20.6 and 31.6 ± 7.8, respectively. HCWs consisted of 12 doctors, 29 nurses, and 180 auxiliary personnel.

The HCWs' working durations were as follows: 44 (19.9%) 0-6 months, 22 (10.0%) 6-12 months, 72 (32.6%) 1-5 years, and 83 (37.6%) over 5 years. Hospitalization durations of the patients were as follows: 111 patients (38.7%) 0-3 days, 81 (28.2%) 3-7 days, 56 (19.5%) 7-14 days, 28 (9.8%) 14-30 days, and 11 (3.8%) more than 30 days.

Information regarding previous antibiotic use within the previous 6 months was available for 178 HCWs; of these 67 (37.6%) admitted antibiotic use while 111 (62.4%) denied it; the remaining 43 could not remember their antibiotic history exactly and so were not included in this analysis. The antibiotic use of patients was 65.5% (188 of 287), which was significantly higher than that of HCWs ($P < 0.05$). No statistically significant difference was found regarding the antibiotic use among HCWs who had been working for less than five years (antibiotic use 37.3%) and more than five years (40.3%) ($P > 0.05$). Vancomycin or cephalosporin use of HCWs and patients were 5.1% and 36.6% respectively ($P < 0.05$).

Of the patients, 74.2% (213) had invasive devices like indwelling catheters, central venous catheters, intravascular lines, Tenckoff catheters, and Foley catheters. There was no statistically significant difference regarding catheterization between surgical departments and medical departments ($P > 0.05$).

Medical history for any kind of surgical intervention within the previous 6 months was 54.7% in patients. Nine patients had a family member working as a HCW.

Presence of co-morbid illnesses, like chronic diseases requiring frequent hospital outpatient/inpatient visits (chronic renal failure, malignity etc.), which predispose to VRE colonization, was higher in medical departments (61.5%) than in surgical departments (40.3%) ($P = 0.04$). The rate of co-morbid diseases that may predispose to VRE colonization was 7.2% among HCWs. Demographic findings and risk factors for VRE carriage are shown in Tables 1 and 2.

Table 1. Demographic findings and risk factors for VRE carriage in HCWs.

	HCWs (n = 221)
Sex (female/male)	92/129
Mean age	50.6
Working durations	
0-6 months	44 (19.9%)
6-12 months	22 (10.0%)
1-5 years	72 (32.6%)
>5 years	83 (37.6%)
Co-morbid diseases*	16 (7.2%)
Antibiotic use within 6 months	67 (37.6%)
Vancomycin or cephalosporin use	9 (5.1%)

*Chronic diseases requiring frequent hospital outpatient/inpatient visits (chronic renal failure, malignity etc)

Table 2. Demographic findings and risk factors for VRE carriage in patients.

	Hospitalized patients (n = 287)
Sex (female/male)	136/151
Mean age	31.6
Hospital time	
0-3 days	111 (38.7%)
3-7 days	81 (28.2%)
7-14 days	56 (19.5%)
14-30 days	28 (9.8%)
>30 days	11 (3.8%)
Co-morbid disease*	151 (52.6%)
Antibiotic use	188 (65.5%)
Vancomycin or cephalosporin use	105 (36.6%)
Family member of HCW	9 (3.1%)

*Chronic diseases requiring frequent hospital outpatient/inpatient visits (chronic renal failure, malignity etc.)

False positive black forming colonies were seen as high as 25% in enterococcosel agar. However, when the black colonies were inoculated into the blood agar media, bile-esculine agar, and other media that include 6.5% sodium chloride, no growth was observed except from in 1 patient who was excluded from the study later on because of his age. That patient was only 2 years old and a rectal swab was taken only because he was in the neurosurgical ICU with other adult patients and recently had been transferred from another hospital. He was positive for VRE rectal carriage, but he had just arrived from another hospital, a children's hospital known to have a high VRE colonization prevalence.

Discussion

Nosocomial VRE outbreaks were first reported in the late 1980s. Since that time, scientific reports of VRE have increased over 20-fold (5). Data on ICU patients from the National Nosocomial Infection Surveillance Study (NNIS) of the Centers for Disease Control and Prevention (CDC) showed that by 1998 nosocomial infections caused by enterococci were 8.1% and there has been a dramatic rise in the percentage of enterococcal isolates resistant to vancomycin—from 0.5% in 1989 to 22% in 1997 among ICU patients with nosocomial infection reported to NNIS (6). However, the rate of increase has diminished: 31% in 2000 compared to 12% in 2003 (6,7). The present study was planned to see the VRE colonization prevalence in our hospital staff and patients, and by doing so to make future plans for hospital infection control. We also wanted to investigate the prevalence of risk factors for VRE colonization that were described beforehand by other studies, to find out our hospital population's characteristics regarding this subject (8-10).

Safdar et al. reviewed the literature for the risk factors that predicted nosocomial colonization or infection with individual multi-resistant organisms including VRE and they found that 7 types of risk factor were most likely to result in colonization or infection with multi-resistant species: advanced age, severity of illness, inter-institutional transfer of the patient, prolonged hospital stay, gastrointestinal surgery, transplantation, exposure to medical devices especially central venous catheters, and heavy exposure to broad-spectrum antimicrobial drugs (8). They also underlined that exposure to other broad-spectrum antimicrobials, such as third-generation cephalosporins and other drugs with anaerobic activity, was more important in promoting colonization and spread of VRE than was the use of vancomycin (8). A Greek study determined cancer, chronic renal failure, length of hospitalization, use of monobactams and carbapenems, and previous ERCP as risk factors for VRE colonization (10). A meta-analysis that controlled for variability in selection of control groups and length of stay revealed only a modest association between vancomycin use and colonization by VRE (12). In the light of these studies, we investigated the presence of risk factors among our study population and found high rates such as antibiotic use for 65.5% and vancomycin or cephalosporin use for 36.6% among our hospitalized patients. Although the rate of antibiotic use in HCWs was lower than that of the patients, still the percentage was a considerable rate with 37.6%. Since we did not have any positive results for VRE, we were not able to compare the vancomycin and cephalosporin effects on colonization.

Patients with a serious underlying disease and a high severity-of-illness score, particularly those who have undergone complicated surgery or who have renal or other organ failure, are at greatly increased risk from multi-resistant organisms (8). Of our hospitalized patients, 54.7% had a past medical history of surgical intervention within the previous 6 months, but none of these surgeries was complicated. Co-morbid diseases like chronic renal failure, diabetes mellitus, or malignity, which may predispose to VRE colonization, were present at a low percentage with 7.2% in HCWs, while it was high with 52.6% in patients; but as we mentioned before, none of them was colonized with VRE.

Invasive devices of all types generally play a far more important role in increasing susceptibility to nosocomial infection than underlying diseases (11). Such devices include intravascular catheters in the case of nosocomial bloodstream infection, urinary catheters with nosocomial urinary tract infections, intubations and mechanical ventilator support with nosocomial pneumonia, and ventriculostomy with nosocomial meningitis (10). Our patients also had a considerably high percentage of invasive devices (74.2%).

Since we aimed to perform an epidemiologic study, here we can discuss the rectal surveillance culture in the absence of an outbreak, whether it was essential or not. Regarding this subject, there are totally 43 studies in the literature that are related to rectal colonization of multi-drug resistant (MDR) bacteria (14). Of these studies, 23 are about rectal colonization of VRE. Mainly these studies have been carried out after an index case or an outbreak. There are only a few studies that have been performed in the absence of an outbreak like in our study (14-16). Among these, Silverblatt et al. and Trabulsi et al. performed their studies with patients carrying a high risk for colonization such as residents of a long-term care facility and pediatric patients (15,16). Silverblatt et al. conducted 2 studies in 2 years and found that 69/200 and 130/230 residents had risk factors for VRE colonization (15). Trabulsi et al. prospectively surveyed 93 high risk pediatric patients (16). Both studies showed no VRE colonization similar to our results. Silverblatt emphasized that the adherence to infection control practices by the patient care staff may be associated with the absence of transmission of VRE colonization among its residents.

In conclusion, every hospital or health center has to decide individually whether to perform rectal carriage of MDR bacteria surveillance. The presence of risk factors does not necessarily mean infection all the time, especially in the absence of an outbreak. VRE colonization was detected neither among HCWs nor hospitalized patients in our study. The possible explanations of this result for hospitalized patients are low inter-institutional transfer, HCWs' being free of VRE colonization (transmission is less likely), the strict infection control strategy of the hospital, isolation of newly transferred patients suspected of having VRE colonization, isolation of VRE colonization identified patients, use of indwelling catheters only when indicated and their early removal, and low prevalence of malignity (since the hospital does not have an oncology unit). The possible explanations of these results for HCWs are as follows: patients' being free of VRE colonization (transmission is less likely); failure to include the target subjects like doctors and nurses, who usually refuse to participate; low vancomycin or cephalosporin use within 6 months; and low prevalence of predisposing chronic diseases (7.2%). The effectiveness of strict hospital infection control programs is very important to prevent colonization even in the presence of risk factors.

Acknowledgements

This project was supported by the Scientific and Technological Research Council of Turkey (TÜBİTAK) with project number SBAG-AYD 493. Special thanks to our laboratory technicians, Nigar BOZDOGAN and Meliha ALBAYRAK, for their help in carrying out the work by supplying and preparing the culture media.

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