LETTER TO THE EDITOR

Surveillance for vancomycin-resistant enterococci colonization among patients of a liver transplant program

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The emergence and spread of multiple-drug resistant enterococci [vancomycin-resistant enterococci (VRE)] has been a worldwide cause of concern [1]. Different studies showed that liver transplant recipients are at increased risk for colonization and infection with these pathogens [2–6]. Other risk factors for VRE acquisition include hospital factors [location in an intensive care unit (ICU), proximity to a VRE colonized patient, extended length of stay in the hospital], antimicrobial use and host characteristics, such as the presence of a hematologic malignancy [1]. Colonization with these pathogens, predominantly of the gastrointestinal tract, usually precedes infection. Surveillance for enteric VRE colonization among liver transplant recipients and other high-risk patients may allow the early identification of colonized patients and the timely adoption of other interventions designed to prevent person-to-person transmission of VRE [1]. In Brazil, acquisition of VRE has been documented in different centers since the first isolation in this country in 1996 [7–11]. In the city of Rio de Janeiro, outbreaks of VRE occurred in different hospitals since 2000. Nevertheless, there are scarce data on the frequency of VRE colonization of high-risk patients in this area. We describe the results of surveillance for enteric colonization with VRE among patients with cirrhosis who were admitted for liver transplantation at a university hospital in Rio de Janeiro, Brazil.

This study was prospectively carried out at Hospital Universitário Clementino Fraga Filho, a teaching hospital affiliated to Universidade Federal do Rio de Janeiro. By the time this study began, VRE had not been isolated in any clinical specimen from infected patients admitted to this hospital and routine surveillance for VRE was not implemented. However, candidates for liver transplantation program were frequently admitted to other hospitals. This fact raised the concern about the possibility of nosocomial acquisition of VRE by these patients in other medical facilities.

Cirrhotic patients admitted for liver transplantation between October 2000 and December 2002 were eligible for the study. Patients were included in this study only after signing an informed consent. Rectal swab specimens were collected within the first 72 h after admission for transplantation. In part of this population, follow-up rectal swab or stool specimens were collected at postoperative weeks 2, 6 and 13. Perioperative antimicrobial prophylaxis consisted of ampicillin plus sulbactam for 48 h. Selective bowel decontamination was not used in any case after transplantation. Additional data were collected in each case by non-structured interviews or review of medical charts. Demographic and preoperative data included: age, sex, Child-Pugh-Turcotte and model for end-stage liver disease (MELD) scores at the time of surgery, hospital admissions and the antibiotics used within the previous 6 months, the occurrence of spontaneous bacterial peritonitis, the diagnosis of liver disease, the presence of diabetes mellitus or renal failure (defined by serum creatinine persistently above 2.5 mg percent at the time of surgery), time spent in the waiting list and invasive procedures that had been carried out before transplantation. The postoperative data variables that were assessed included the antibiotics that were used for at least 72 h, the need for hemodialysis or for a new laparotomy, the length of stay in the ICU and the total length of hospital stay.

Swab and stool specimens were inoculated onto Enterococcosel agar (Becton Dickinson, Cockeysville, MD, USA) containing vancomycin (8 μg/ml). Plates were incubated at 37 °C for up to 3 days. Each morphologically different colony resembling *Enterococcus* was further characterized by means of standard biochemical tests (bile-esculin test, salt tolerance test in 6.5% NaCl brain-heart infusion (BHI), hydrolysis of arginine), observation of motility in semisolid motility medium and pigment production on Mueller Hinton agar [12]. Vancomycin susceptibility was tested by the disc diffusion method according to National Committee for Clinical and Laboratory Standards (NCCLS) guidelines. This study was approved by the Institutional Research Board.

Eighty-two subjects were included in the study. Forty (49%) of them were men. The median age was 51 years (interquartile range: 42–59). The most common diagnoses of liver disease were: chronic hepatitis C ($n = 33$, 40%), hepatocellular carcinoma ($n = 13$, 16%), primary sclerosing cholangitis ($n = 9$, 11%), auto-immune hepatitis

($n = 7$, 9%) and cryptogenic cirrhosis ($n = 6$, 7%). Ten patients (12%) had diabetes mellitus and none had renal failure at the time of surgery. During the 6 months that preceded liver transplantation, 33 (40%) patients were admitted to this or to other hospitals and 42 (51%) subjects received antibiotic treatment. Twenty-one patients (26%) were treated with norfloxacin for secondary prophylaxis of spontaneous bacterial peritonitis. The other antibiotics used during that period were: ampicillin (four cases), cefalosporins (eight cases), levofloxacin (five cases), rifampin (three cases), metronidazol (three cases) and oral neomycin (six cases). Forty-two patients (51%) had Child-Pugh-Turcotte score ≥10. The median MELD score was 18 (range: 7–37). The median time spent in the waiting list was 363 days (range: 50–880 days). A transjugular intrahepatic portosystemic shunt had been inserted in two patients. One patient with hepatocellular carcinoma had been submitted to partial hepatectomy. Other four patients with hepatocellular carcinoma had been treated with chemoembolization. None of these 82 patients had a positive surveillance culture for VRE on admission for transplantation.

Postoperative surveillance cultures were performed in 50 liver transplant recipients. Twenty-eight of these patients (55%) received antibiotic therapy after transplantation. The median number of antibiotics used in these cases was two. Ciprofloxacin ($n = 16$, 32%), vancomycin ($n = 12$, 24%), imipenem ($n = 8$, 16%), piperacillin plus tazobactam ($n = 8$, 16%), cefepime ($n = 8$, 16%) and metronidazole ($n = 7$, 14%) were the most frequent antimicrobial drugs used. Four patients (8%) had renal failure and were treated with hemodialysis. Sixteen patients (32%) were submitted to a new laparotomy. The median length of stay in the ICU was 4 days (range: 2–40 days). The median length of hospital stay was 13 days (range 9–106 days). The median follow-up time from transplant surgery until the last surveillance culture was 38 days (interquartile range: 9–172 days), adding up 101 follow-up cultures (median of two per patient). Enteric carriage of VRE was not detected in any of these patients.

In a few similar studies, the prevalence of colonization ranged from 3% to 14% among patients who were waiting for or who had been admitted for liver transplantation [5–6,13]. In the study of Bakir *et al.* [6] postoperative nosocomial acquisition of VRE occurred in 12 (44%) of 27 admissions of liver transplant recipients. These findings contrast with the absence of isolation of VRE in this study. Our results suggest that the prevalence of colonization in this group of patients remains low, despite the increasing detection of VRE in different hospitals in this region. A lower frequency of exposure to risk factors for VRE colonization may possibly explain the difference between our findings and those reported by other authors [5–6,13]. Particularly, a lower 'colonization pressure' [14] at the site where this study was carried out may have probably influenced its results.

The use of surveillance cultures for the detection of unrecognized carriage of VRE targeted to high-risk patients, including liver transplant recipients, has been recommended as a fundamental component of the strategy to prevent introduction and propagation of VRE in medical facilities [15]. In fact, most patients with unrecognized colonization will never develop infection but will persist as a reservoir for VRE transmission for prolonged periods [5]. The absence of postoperative acquisition of VRE among our patients do not support the routine implementation of periodic surveillance cultures after liver transplantation at our center at this time. Nonetheless, in view of the ongoing dissemination of VRE in other medical facilities in this area, on-admission surveillance appears to be indicated for all liver transplantation candidates and recipients at our center. Further studies are needed to set up predictive rules that would allow targeting on-admission surveillance to subjects under higher risk of VRE colonization. Targeting surveillance to high-risk liver transplant patients may improve the cost-effectiveness of this intervention.

The results of our study underline the important geographic variation in the prevalence of VRE colonization, and the need to adapt the strategies for the control of VRE dissemination among liver transplant recipients according with the local epidemiology of these pathogens because of the costs associated with surveillance.

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