Significance of vancomycin resistant enterococci from urinary specimens at a tertiary care centre in northern India

Neelam Taneja, Phulan Rani, Rekha Emmanuel & Meera Sharma

Department of Medical Microbiology, Postgraduate Institute of Medical Education & Research, Chandigarh, India

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Background & objectives: There is a paucity of information on vancomycin resistance in enterococci from India. In the present study, enterococci isolated from urine specimens were screened for vancomycin resistance.

Methods: 144 enterococci isolates obtained in pure and significant numbers (>10^5 cfu/ml) from 9664 urine specimens were subjected to agar screen method of National Committee for Clinical Laboratory Standard (NCCLS) for presence/absence of vancomycin resistance. Minimum inhibitory concentration (MIC) was performed by E-test and agar dilution method.

Results: Eight vancomycin resistant enterococci (VRE) were obtained, namely, 5 Enterococcus faecium, 1 each of Enterococcus faecalis, E. casseliflavus and E. pseudoavium. The MIC ranged from 8 to 32 µgm/ml. The records of these 8 patients were retrospectively reviewed for clinical details. Five patients had nosocomial urinary tract infection (UTI), while in 2 patients UTI was community acquired. One patient had asymptomatic bacteriuria. Two patients with nosocomial UTI developed clinical sepsis and died in spite of vancomycin treatment. Urinary catheterization, surgery on genitourinary tract, prior exposure to third generation cephalosporins and metronidazole were present in 6, 5, 3 and 2 patients respectively.

Interpretation & conclusion: Although the frequency of isolation of VRE is not very high in our setting as compared to West, this may just be the beginning of the problem. Screening for vancomycin resistance is recommended in all patients with suspected UTI who have significant bacterial counts.

Key words: India - urine - vancomycin resistant enterococci

 Enterococci are primarily opportunistic pathogens. Progress in medical technology and intensive use of broad spectrum antibiotics in the hospitals have been responsible for emergence of these organisms as important nosocomial pathogens1. Since the first report of vancomycin resistant enterococci (VRE) in 1988 by Uttley et al2, the VRE have spread rapidly in the West. From 1989 to 1993 the percentage of nosocomial infections due to VRE reported to the Centers for Disease Control and prevention, USA increased from 0.3 to 7.9 per cent3. Though the major problem in treatment of VRE infection arises in endocarditis, the urinary tract is the commonest site from where bacteraemia can occur. There are very few reports on isolation of VRE from India4. Though epidemiology of nosocomial VRE bacteraemia has been quite extensively studied5-7, studies on problems posed by the VRE as pathogens in urinary tract infection (UTI) are very few8. Enterococci in mixed culture are very commonly isolated from urine samples. It is not always easy to assess the clinical significance of VRE in routine culture or to differentiate colonisation from infection. Therefore, the
present study was undertaken to look for vancomycin resistance in enterococci obtained in significant numbers from urine samples at a tertiary care centre in northern India, and to study the role of these organisms as UTI pathogens.

A total of 9664 urine (midstream, catheter) specimens collected from patients suspected to have UTI were cultured on cysteine lactose electrolyte deficient medium (CLED) (Hi-Media Laboratories, Mumbai, India) during October 2000 to April 2001 in the Department of Medical Microbiology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh. Gram-positive catalase negative cocci (n=164) isolated in significant counts (> 10^5 cfu/ml) in pure culture were included in the study. Identification of isolates up to the species level was done according to the conventional scheme of Facklam and Collins9. Screening for vancomycin resistance was done by agar screen methods10 on both Mueller-Hinton agar (MHA) and brain heart infusion agar (BHI) (Difco Laboratories, Detroit, USA). Minimum inhibitory concentration (MIC) of vancomycin was performed by E test (AB Biodisk, Solna, Sweden) and agar dilution method of National Committee for Clinical Laboratory Standards (NCCLS)10 using both BHI and MHA. Plates were incubated at 35°C for 24 h. The susceptibility to other antimicrobial agents was estimated by the disc diffusion method11 on BHI agar. The antibiotics used were: teicoplanin (30µg, Oxoid Ltd. Hampshire, England), amoxycillin (30µg), penicillin (10U) and vancomycin (30µg), (Hi-media Laboratories, Mumbai, India). Enterococcus faecalis ATCC 29212, purchased from Becton-Dickinson, India was used as control strain. The record of the patients revealed that there was no prior exposure to vancomycin in any of the patients. In the present study, 55 per cent of enterococci were Enterococcus faecalis followed by Enterococcus casseliflavus (23.6%) and E. faecium (11.8%). This difference may be due to geographical variation.

The MIC of the VRE ranged from 8-16 µg/ml by the E test and 8-32 µg/ml by the agar dilution method. All isolates were susceptible to teicoplanin. Only 4 isolates could be picked up by the 30 µg disc of vancomycin in the disc diffusion susceptibility testing. Based on the results of the MIC studies and susceptibility to teicoplanin, it appears that Van B may be the phenotype for E. faecalis and E. faecium. The low level resistance shown by E. casseliflavus appears to be Van C type. Confirmation of these results at genetic level by PCR is required.

Of the 8 patients with VRE, 4 females, 4 males, age 25 to 70 yr, 5 developed nosocomial UTI, two had community acquired UTI and 1 asymptomatic bacteriuria. The length of hospitalization for symptomatic patients with nosocomial UTI ranged from 8 to 37 days with an average of 20.5 days. Two patients with nosocomial UTI developed clinical symptoms of sepsis and died. E. faecium were isolated on multiple occasions from urine samples of these patients but not blood. They were treated with vancomycin as enteroocci were found to be susceptible to vancomycin on disk diffusion susceptibility tests. The record of the patients revealed that there was no prior exposure to vancomycin in any of the patients. In four of the symptomatic patients (2 each with nosocomial and community acquired UTI), the organisms cleared with simple drugs like nitrofurantoin, amoxycillin and ciprofloxacin. In the patient with asymptomatic bacteriuria, organisms disappeared after removal of the catheter and ampicillin therapy. Antibiotic selective pressure exerted
by extensive use of third generation cephalosporins and drugs with potent activity against anaerobes have been reported to predispose to VRE colonization and infection\textsuperscript{1,5,12}. In the present study prior exposure to third generation cephalosporins and metronidazole occurred in 3 and 2 patients respectively. Animal studies suggest that the cephalosporins predispose to establishment of VRE colonization and antianaerobic drugs like metronidazole might favour persistence of high levels of VRE colonization\textsuperscript{12}. Studies on epidemiology of nosocomial UTI caused by vancomycin susceptible enterococci have shown urinary catheterization to be an important predisposing factor present in 82 to 95 per cent of patients\textsuperscript{13,14}. However, in another study it was found that only 31 per cent patients with nosocomial UTI due to VRE were catheterized\textsuperscript{8}. In the present study, 4 of the 5 patients with nosocomial UTI were catheterized and three had an indwelling catheter for more than seven days. Though the frequency of isolation of VRE was not very high in our setting compared to the West, it appears that this may just be the beginning of the problem. Since 2 of the 8 patients with UTI due to VRE developed clinical sepsis and died inspite of vancomycin therapy, screening of symptomatic patients with significant isolates of enterococci obtained in pure culture is recommended.

References