Vancomycin Resistant Enterococci (VRE)

253. Clinical Features and Risk Factors of Co-colonization of Methicillin Resistant Staphylococci and Vancomycin Resistant Enterococci

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Background: The glycopeptides have traditionally been the mainstay of treatment of methicillin-resistant *S. aureus* (MRSA), but overuse has led to the emergence of vancomycin-intermediate and vancomycin-resistant *S. aureus* (VISA and VRSA, respectively). Recent reports support the transfer of genetic material among bacteria as contributing to the development of VRSA. Therefore, the co-colonization of methicillin-resistant staphylococci (MRS) and vancomycin resistant enterococci (VRE) may facilitate the emergence of VRSA due to proximity of location for transfer of transposons or plasmids which carry the genes that express vancomycin resistance such as *van*A.

Objective: We analyzed clinical features and risk factors of co-colonization of MRS and VRE.

Methods: We performed the retrospective cohort study and reviewed the medical records of patients whose culture were positive for VRE from Jan. 2006 to Dec. 2006 at Severance hospital. Co-colonization was defined as VRE and MRS were all positive in culture which was performed in the same clinical specimen at the same time. To evaluate for risk factors of co-colonization, we performed case-control study. The case group was composed of patients with co-colonization and controls were selected to match the case patients for age, sex and site of isolation among patients with only VRE.

Results: Among 500 VRE positive patients, total 33 (6.6%) had co-colonization of VRE and MRS. The mean age of 33 patients was 55.4 ±16.5 years. The most common isolated site was wound (N=9, 27.3%) followed by urine (N=8, 24.2%). The staphylococcal species cultured with VRE were 18 MRSA (54.5%) and 15 methicillin-resistant coagulase negative staphylococci (45.5%). The most common major underlying disease was solid cancer (N=10, 30.3%). 20 patients (60.6%) had the prior hospitalization history within 1 year from co-colonization and the mean cumulative hospital days (HD) was 84.6 ± 55.9 days. The mean duration from current admission to co-colonization was 48.8 ± 51.2 days. The case group had significantly longer mean cumulative HD within 1 year than the control group (82.67 ± 57.68, 35.71 ± 15.32 days, p=0.001) and the only risk factor of co-colonization was the mean cumulative HD within 1 year in multivariate logistic regression analysis (OR=1.04, 95% CI: 1.01-1.07, p=0.006).

Conclusions: We confirmed that there were co-colonization of MRS and VRE which were cultured from the same clinical specimen at the same time. The mean cumulative HD within 1 year was significantly associated with co-colonization. The active surveillance of co-colonization of MRS and VRE should be performed continuously to prevent the emergence of VRSA due to horizontally transferability.

254. Risk Factors for VRE Bloodstream Infection in Pediatric Patients

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Background: Enterococcal bloodstream infections (BSI) cause morbidity and mortality in hospitalized children. Because vancomycin resistant enterococcus (VRE) is resistant to multiple antibiotics, it can be difficult to treat. There is a paucity of data regarding enterococcal BSI in children. Specifically, the risk factors for VRE have not been elucidated in children.

Objective: To determine the risk factors associated with VRE BSI in hospitalized children.

Methods: We conducted a case-control study using data from the Children's Hospital of Philadelphia from 2001-2006. Eligible patients were identifed from the microbiology laboratory records. All patients with VRE BSI were compared to patients with VSE BSI. Demographic and clinical data were collected by retrospective chart review using a structured data collection tool.

Results: There were 347 patients with enterococcal BSI. 39 were VRE, 308 were VSE. VRE was more likely to be speciated as faecium (79% vs.12%) than faecalis, and to be ampicillin resistant (61% vs 4%) and high-level gentamicin resistant (23% vs 7%). Out of 212 isolates tested for linezolid susceptibility, 10 isolates were resistant and 18 isolates were intermediate; all were VSE. On multivariable analysis, age greater than 3 years (OR 3.67, 95% CI 1.80-7.51) and neutropenia (OR 4.54, 95% CI 1.89-10.90) were identified as independent risk factors for VRE BSI.

Conclusions: Age at bacteremia greater than 3 years and presence of neutropenia at onset of bacteremia were significantly associated with increased risk for an enterococcal BSI caused by VRE.

255. Clinical Risk Factors for Infection with Linezolid Non-Susceptible Enterococci

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Background: Multiple case reports of enterococcal linezolid resistance have been published, but clinical risk factors for infection with these isolates remain understudied.

Methods: All patients with linezolid non-susceptible enterococci (LIRE) from 2003 - 2006 were identified at an academic medical center. Each case was matched to 4 randomly-selected hospitalized controls concurrent with the date of LIRE culture.

Demographic, pharmacy, laboratory, and clinical outcome information were compared using conditional logistic regression.

Results: 15 patients with LIRE and 60 controls were identified. Cases and controls did not significantly differ by age, sex, or race. Four (26.7%) cases had positive LIRE cultures within 48 hours of admission, and of these, all had been previously admitted to the hospital within the past 30 days. Of the 11 cases that had positive LIRE cultures 48 hours or more post admission, 45.5% had been admitted within the previous 30 days. Ten (66.7%) LIRE isolates displayed intermediate resistance to linezolid with the remainder being classified as resistant. 53.3% of LIRE were isolated from blood cultures, 26.7% from urine cultures, and the remaining 20% from other sources. Linezolid use during the at-risk time period (OR=13.16, 95% CI: 1.13, 153.49) and admission to a medical service (OR=10.99, 95% CI: 2.03, 59.42) were independently associated with LIRE culture positivity. Use of vancomycin, cephalosporins, or any antibacterial during the at-risk period were not found to be independent predictors. Among LIRE cases, there was 33.3% in-hospital mortality and a 40% readmission rate within 30 days.

Conclusions: Few studies have examined risk factors for the acquisition of LIRE, which may differ from the risk factors for vancomycin-resistant enterococcal infections. While the prevalence of LIRE remains low, additional research is needed to understand its emergence and limit its spread. Multi-institutional observational studies are needed to achieve the power necessary to further study risk factors for LIRE.

256. Timing Of Recontamination Of The Environment On A Newly Renovated Hospital Ward With Vancomycin-resistant *Enterococcus* And Methicillin-resistant *Staphylococcus aureus*

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Background: Numerous studies have demonstrated that environmental contamination is common in the rooms of patients colonized or infected with methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE). However, less information is available regarding the levels of contamination in other areas of hospital wards, and few studies have examined the rate of recontamination of clean surfaces. In our institution, relocation of patients to a newly renovated medical ward provided an opportunity to study the rate of recontamination of the ward environment.

Objective: To examine the rate of recontamination of the environment with MRSA and VRE on a newly renovated medical ward that conducted active surveillance and isolation for MRSA but not for VRE.

Methods: Culture surveys for MRSA and VRE were performed on the old medical ward and on the new ward prior to the move and days 2, 6, 9, 14, 20, 54, and 93 after the move. Cultures were collected from MRSA isolation rooms, non-isolation rooms, and from physician and nurse work areas. To assess the rate of

recontamination with MRSA in isolation rooms, serial cultures were obtained for 36 patients 1, 3, and 7 days after surfaces were disinfected.

Results: On the old medical ward, 5 of 16 (31%) non-isolation rooms and 3 of 12 (25%) physician and nurse work areas were contaminated with VRE, whereas only 1 of 16 (6%) non-isolation rooms and 1 of 12 (8%) work area sites were contaminated with MRSA. On the new ward, the proportion of non-isolation rooms contaminated with VRE increased gradually to the same level as the old ward by day 93 (33%) and VRE was sporadically isolated from work areas (0 to 14% of sites positive). MRSA was isolated infrequently from non-isolation rooms (0 to 11% positive), and no cultures from work areas were positive for MRSA. Within 1 day after disinfection of surfaces in MRSA isolation rooms, 11 of 28 (39%) rooms had positive environmental cultures for MRSA, and similar proportions of rooms were positive at 3 and 7 days after disinfection (41% and 50%, respectively).

Conclusions: In a hospital that conducts surveillance and isolation for MRSA but not VRE, rapid recontamination of the environment with MRSA occurred in isolation rooms, whereas contamination of a new ward was uncommon in non-isolation rooms and negligible in physician and nurse work areas. VRE contamination increased steadily in patient rooms on the new ward and nearly one-third were contaminated 93 days after the move.

257. The Attributable Cost of Enterococcal Bloodstream Infections in a Non-Surgical Hospital Cohort

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Background: Blood stream infections (BSI) are a significant cause of hospital morbidity, mortality and cost. It is important to quantify the cost of these infections and identify the attributable cost of antibiotic resistance.

Objective: To determine the attributable cost of vancomycin-sensitive and resistant enterococcal (VSE, VRE) BSI in hospitalized patients using administrative data.

Methods: This study was conducted at a 1250-bed, academic medical center. All non-surgical patients admitted during 2002 and 2003 for > 48 hours were included. BSIs were identified using the hospital Medical Informatics database. The first episode of VRE or VSE BSI during the hospital admission was analyzed. Patients with no history of enterococcal BSI served as the comparison group; one admission was randomly selected for patients with multiple admissions. ICD-9-CM diagnosis codes were collected for all admissions in the past 2 years; ICD-9 procedure codes were collected for the current admission only. Comorbidity and procedure variables were created from ICD-9-CM codes and defined using the HCUP Clinical Classifications Software. Cost data were obtained from the hospital Trendstar accounting database and inflation adjusted to 2003 dollars. Ln-transformed costs were used as the dependent variable in a multivariate generalized least squares model to determine attributable costs.

Results: The cohort included 21,154 pts; 276 (1%) had an enterococcal BSI [94 (34%) VRE, 182 (66%) VSE] and 20,079 (95%) had no BSI. Patients with an enterococcal BSI had a longer median hospital LOS than those without BSI [12 days vs. 5 days (p<.001)], were more likely to spend time in an ICU [103 (37%) vs. 3,330 (16%); p<.001] and more likely to die in the hospital [61 (22%) vs. 845 (4%); p<.001]. Patients with VRE BSI had significantly higher unadjusted costs (median $35,648; range $5,706-$334,901) compared to those with VSE BSI (median $17,691; range $3,063-$218,594) (p<.001) and those without BSI (median $7,059; range $714-$273,305) (p<.001). Both VRE and VSE BSI were independent predictors of hospital costs (p<.001) in the multivariate regression model, after controlling for 65 significant cost predictors, including underlying comorbidities, procedures, non-enterococcal BSI, patient age and mortality (adjusted R^2 = .378). The attributable cost of VRE BSI at $3,161 (95% CI $2,739-$3,647) was significantly higher than the attributable cost for VSE BSI at $1,745 (95% CI $1,513-$2,014) (p=.009).

Conclusions: The attributable cost of VRE BSI is significantly greater than VSE BSI. However, these costs are lower than previously reported. The use of administrative data to conduct this large cohort analysis is a strength of this study and should help determine comparable cost estimates across hospitals.

258. Annual Trends of Incidence of Vancomycin-Resistant *Enterococci*(VRE) in a Tertiary-Care Teaching Hospital

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Background: Vancomycin-resistant *enterococci* (VRE) is one of the common nosocomial pathogens. The annual incidence of VRE has increased gradually. However, there are few institutional long-term studies to describe clinical characteristics, annual trends of resistance and the effect of infection control program for VRE.

Objective: The objective of this study is to describe the annual trends of vancomycin-resistant rate of *enterococci* isolates and incidence density rate of VRE during 9 years from 1998 to 2006 in a tertiary-care teaching hospital in Korea.

Methods: A total 261VRE isolates which were the first isolates of a given species per patient were identified from January 1 1998 to December 31 2006. Clinical information and microbiologic data were collected by medical records, OCS (order communication system) and VRE surveillance worksheet retrospectively. Data was analyzed by SPSS 12.0 (SPSS Inc., Chicago, IL) and Epi-Info Ver. 6.0 STATCALC software.

Results: The rate of VRE among *enterococcus* species were 0.25% in 1998 but increased gradually up to 14.62% in 2005. Annual trend of VRE incidence density rate (incidence/10,000 patient-days) over 9 years was significantly increased; 0.03, 1998; 0.59, 2002; 1.75, 2004; 2.62, 2005; 2.34, 2006 (p=.00). Infection control program for VRE has been implemented since January 2004. However, VRE rate

significantly increased in 2004 and 2005 but showed a slight decrease in 2006. All of the infections were hospital acquired infections (mean of hospital days: 57.1), and 62.5 percent of the patients had a history of ICU stay. Fifty-three percent of the patients had a surgery during the admission, and among which 53% had a neurosurgical procedures. Ninety-five percent of the patients received antibiotics within 1 month [3rd cephalosporins (70.9%), aminoglycosides (55.6%), glycopeptides (25.7%)]. *E. faecium* expressing VanA phenotype was the most prevalent (70.8%).

Conclusions: This study provided the annual resistant rate and incidence rate of VRE during long-term period. We identified it is necessary to reinforce VRE infection control program including strict isolation precaution and environmental control to decrease VRE isolates.

259. Intensive Control Strategies to Reduce the Incidence of Vancomycin-Resistant Enterococci (VRE) on a Hematologic Malignancy Service (HMS)

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Background: Vancomycin-resistant enterococci (VRE) have become increasingly important nosocomial pathogens in immunocompromised hospitalized patients. Despite the use of active surveillance and contact isolation for VRE among the Hematologic Malignancy Service (HMS) patients at our institution 20% of HMS patients became colonized with VRE between May 2004 and February 2006, with bacteremia developing in 19% of colonized patients.

Objective: We describe here the implementation and outcome of an intensive intervention aimed at decreasing new VRE colonization in this vulnerable population. Methods: Enhanced control strategies began in March 2006 with contact isolation of new admissions until VRE screen returned negative. Administrative championship of the VRE intensive strategy allowed for the hiring of staff to monitor compliance with hand hygiene as well as increased funding for environmental services (EVS) to improve cleaning in the HMS; a fluorescent gel was used to assess EVS cleaning effectiveness. Mandatory education and competency assessments with feedback for EVS staff were provided.

Results: Despite continued high colonization pressure, implementation of the intensive intervention was associated with a decrease in the mean nosocomial VRE incidence rate from 7.24 (pre-intensive intervention, June 2004-February 2006) to a post-intervention (March 2006 - February 2007) rate of 4.63 per thousand patient-days (SD 3.43 and 2.61, respectively). Monitors were able to document sustained > 90% adherence to hand hygiene and glove use compared to the 60% baseline measurement. Quality control checks of high touch environmental services were improved.

Conclusions: A sustained trend of decreasing nosocomial VRE incidence in the HMS was achieved only after implementation of multiple intensive strategies. These strategies required significant time commitments on the part of multiple staff and additional financial support. In order to be maximally effective, strategies to control

multi-drug resistant organisms requires a partnership between multiple areas of the organization, including hospital administration, laboratory, EVS, infection control, as well as nursing and physician staff.

260. Duration Of Colonization With Vancomycin-resistant *Enterococcus* (VRE)

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Background: Little is known about the duration of VRE carriage and when from an infection control viewpoint de-isolation can be endorsed. In Singapore General Hospital (SGH) VRE carriage is deemed indefinite without any clearance testing thereby stressing limited isolation rooms.

Objective: To determine the duration of VRE colonization among carriers colonized during an outbreak of VRE in SGH in March 2005 (n=176).

Methods: These patients were identified from the hospital database and contacted for the study from 1st July to 31st December 2007. VRE cultures from rectal swabs were obtained with consent at least a month apart and up to a maximum of 3 swabs per patient. Pulsed-field gel electrophoresis (PFGE) was performed to determine whether recurrent VRE strains were the same clone as the previous colonizing strain. The duration of VRE persistence was defined as the interval between the initial positive culture during the outbreak and the last positive culture identified during the study. The mean number of hospital admissions and mean length of total hospital stays (LOS) after the initial detection and before the day of the collection of the first study rectal swab were derived. Antibiotic use in the 6 months prior to the first study rectal swab was derived from medical records.

Results: Of 109 (67 had died) eligible patients, 41 were contactable of who 9 refused. Thirty-two patients had 61 follow-up cultures. The first follow-up culture, collected a mean of 858 days (range, 652 to 995 days) after the initial positive isolate, was negative in 94% (30 of 32). VRE was persistently positive in only 2 patients (6%; persistent duration of 864 and 909 days). PFGE confirmed the same clone as the previous colonizing strain. After 1 negative follow-up culture, the next one was negative in 81% of the patients (17 of 21; 4 refused second swab). After 2 negative cultures, 91% remained culture-negative (10 of 11; 1 refused third swab). There was no significant difference in mean age (81 Vs 66; p=0.11), recent antibiotic use (p= 0.15), mean number of hospital admissions (3 Vs 2; p= 0.67) and mean LOS (27 Vs 16 days; p=0.61) between VRE negative and persistently positive cases.

Conclusions: VRE clearance may be feasible by 3 sequential negative cultures at least a month apart in the majority of VRE carriers. This is especially useful in a setting with limited isolation facilities. However the small size of this study suggests exercising ongoing caution in those who continue to have hospital admissions and antibiotic use.

261. Can Irish Hospitals Implement National Guidelines On The Control & Prevention Of MRSA?

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Background and Methods: Irish guidelines on the control and prevention of methicillin resistant *Staphylococcus aureus* (MRSA) were last published in September 2005. During the consultation process, concern was expressed that compliance would not be possible in many hospitals, due to deficiencies in physical resources, and personnel. In 2007, a questionnaire on the implementation of these guidelines was forwarded to 60 acute hospitals to establish progress and what challenges remain.

Results: Forty-nine (83%) hospitals, broadly representative of Irish acute hospitals, responded. Thirty-six (73%) had a hospital strategic plan that included infection prevention and control (IPC) and of these, 26 (72%) incorporated the national MRSA guidelines. Thirty three (67%) had an annual infection control plan, with 31 (94%) of these incorporating the national MRSA guidelines. 43 (88%) hospitals had major barriers to the implementation of the national MRSA guidelines.

These included:

• inadequate hospital infrastructure, e.g. only adequate in one (2%) hospital to allow full implementation
• laboratory resources only adequate in 3 (6%) hospitals
• infection control staffing only adequate in 15 (31%) hospitals
• availability of single rooms only adequate in 3 (6%) hospitals
• high bed occupancy impacting on guideline implementation in 46 (94%) hospitals

MRSA surveillance takes place in 47 (96%) hospitals with 41 participating in the European Antimicrobial Resistance Surveillance System. In 45 (92%) hospitals, hand hygiene education occurs, with audit results available in 30. Thirty-three (67%) and 39 (80%) hospitals, eradicated MRSA colonization in surgical patients with a prosthesis and in intensive care patients, respectively. Only 13 hospitals had 2.9 metres or more between beds (the recommended space in the MRSA national guidelines), 5 had a ratio of single rooms beds to total beds of 1:3 and 3 hospitals had an MRSA cohort area. Only 33 (67%) hospitals have an antibiotic policy and 17 (35%) an antibiotic stewardship programme.

Conclusions: Major challenges, including significant physical infrastructure deficits, remain in ensuring full implementation of Irish MRSA guidelines. Almost a quarter of hospitals do not include IPC in the hospital strategic service, almost a third of hospitals do not produce an annual IPC plan, 8% do not have hand hygiene education, and 33% do not have a written antibiotic policy.. Our findings must guide further political and other developments in improving patient care and safety and in reducing all healthcare-associated infection, infections caused by MRSA.