Mortality Attributable to VREF in Inpatient Setting

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A. Introduction

First noted in Europe in 1986, vancomycin-resistant enterococci faecium/faecalis (VREF) spread to the United States in 1988. Urinary tract infections are by far the most common enterococcal. infections in humans (16%). Wounds, usually intraabdominal or pelvic (13%), and then bacteremia(8%) are the second and third most common infection caused by enterococci. Enterococci have always been among the more resistant microbes. Their intrinsic genetic constitution has rendered them resistant to a nuniber of antimicrobial agents, and they have proved adept at acquiring other forms of resistance.

Risk factors for acquisition of VREF include patients who are hospitalized for prolonged periods, patients resident on intensive care, transplantation and oncology services, receipt of vancomycin or ciprofloxacin, and a high score on the Acute Physiology and Chronic Health Evaluation H (APACHE H). The Centers for Disease Control and Prevention reported a 20-fold increase nationwide in the percentage of nosocomial enterococci resistant to vancomycin between 1989 and 1993. This increase was even more dramatic among nosocomial enterococci isolated from patients in the intensive care unit (34-fold).

My objectives are to

1. define the attributable mortality per hospital days due to isolation of colonized VREF patients while carefully taking into account episodes with no clinical significance.
2. generate data that can be used to persuade nursing homes and/or other institutions that patients should be re-accepted once their medical problem has been addressed regardless of their VREF status.
3. demonstrate that patients are better cared for off isolation and are more satisfied with their hospital course the shorter there length of stay.
4. secondarily determine risk factors for colonization or infection at CPMC and the nursing stations with the highest conversion rates, the correlation of bacterial load with risk of colonization/infection, patient satisfaction, and hospital readmission.

B. Overview of Study Design

This will be a double blind, randomized trial of nursing home and/or other institutionalized patients who are colonized with VREF either on admission or during their hospital stay. These colonized patients will be divided into two random groups, A and B.

The antibiotic susceptibility of group A VREF will be determined by standard methods and treated appropriately for 7 days and 14 days with intravenous antibiotics while these patients are on isolation. These patients would then be recultured at two weeks and six months post treatment from the initially culture positive site(s) and stool.

Group B would be placed on isolation in the usual manner and would not receive antibiotic intervention. Only their index medical presentation would be addressed. These patients would also be recultured at two weeks and six months post treatment from the initially culture positive site(s) and stool.

A control Group C would be recruited from patients admitted to the hospital who are from nursing home and/or other institutions who are not VREF colonized or infected. These patients would be off isolation. This group would be related to A and B in having similar medical problems and be on the same nursing stations.

All three groups would be accessed for patient satisfaction at the time of hospital diseharge using the nonstandard Duffus patient care observational scale. The records will be compiled for each patient at the time of entry into the study and will include data on (1) the development and grade of decubiti (2) occurrence of other nosocomial infections (3) timing of medications.

a. Definitions

Cases were defined as all hospitalized patients with VREF isolated from any source between June 20, 1997 to January 20, 1998. The patients were identified from the records of the clinical microbiology laboratory. AVRE isolate is any member of the genus Enterococcus resistant to vancomycin with a minimal inhibitory concentration (NffC) of at least 32 ug/ml. Infected patients will be excluded from the study.

VRE infection is defined as the presence of VRE in tissues or body fluids along with signs and symptoms of infection or the presence of VRE in normally sterile body sites or fluids (usually but not necessarily with symptoms of infection).

Colonization is the presence of VRE as a sole isolate 'in body fluids or tissues (eg. sputum, urine, wounds, or the gastrointestinal tract) without clinical signs of infection. The presence of VRE in body fluids or tissues along with other microorganisms that could account for the patients clinical condition is considered to be of unknown significance.

APACHE H was the best predictor of death in patients with an enterococcal infection. This composite score reflects both the severity of acute illness and a patients prior health status and has been adapted for use in a non-ICU setting.

Weighted comorbidity inde (WCI) was the second best predictor of death in patients with an enterococcal infection.. This weighted prognostic scoring system originally was designed to assess the relationship between comorbidity and death in longitudinal studies.

b. Chart reviews

Hospital records were reviewed to obtain demographic and clinical. information. Nficrobiologic records were reviewed to obtain information on the source and drug susceptibility pattern of the isolate. Specific information was obtained regarding the treatment of patients with vancomycin and third-generation cephalosporins; given alone or in combination before specimen collection.

C. Bacteriologic method

Enterococcocal species were identified by standard methods, including Grarn staining, testing for the ability to grow in 6.5% saline solution, the ability to blacken bile esculin medium and motility testing. Antibiotic susceptibility testing will be performed by the Kirby-Bauer disk-diffusion method with final confirmation of vancomycin resistance established by agar dilution, with values greater than 32 ug/ml being considered resistant.

D. Statistical analyses

Both the APACHE 11 and the WCI scoring systems will be used to assess the patients state of health at admission independently of their primary diagnosis. Both the APACHE H score and WCI score will be calculated from information recorded in the medical record within the first 24 hours of admission and recorded as a baseline. Both scores will be repeated again at day 7, day 14 and six months enabling an analysis of covariance.

The primary end point will be attributable mortality of VREF colonization per hospital days. The Kaplan-Meier method with death used as a censoring mechanism will be used to analyze the three groups. The point estimate at day 14 will be used to test the null hypothesis that the incidence of death was same in the patients on isolation. Greenwoods formula will be used to estimate the variances.

Secondary endpoints include risk factors for colonization/infection, conversion rates, bacterial load in reducing colonization/infection, and hospital readmission rates.

E. Subjects

Patients who are infected with VREF will be excluded from the study. It is clear that patients who exhibit signs and symptoms of disease and have antibiotic susceptible bacterium must be treated and it would be unethical to include them in nontreatment group. Patients will be enrolled if they can give verbal consent. The subjects will be recruited fr6m nursing homes or institutionalized patients admitted to the hospital. This study will include 50 patients per group.