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ORIGINAL ARTICLE

Correlation between antimicrobial consumption and incidence of health-care-associated infections due to methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci at a university hospital in Taiwan from 2000 to 2010

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KEYWORDS
Antimicrobial resistance;
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Methicillin-resistant *Staphylococcus*

Objectives: This study was conducted to investigate the correlation between antibiotic consumption and the incidence of health-care-associated infections (HCAIs) caused by methicillin-resistant *Staphylococcus aureus* (MRSA) (HCAI-MRSA) and vancomycin-resistant enterococci (VREs) (HCAI-VREs) at a university hospital in Taiwan during the period from 2000 to 2010.
Methods: Data on annual patient-days and annual consumption (defined daily dose/1000 patient-days) of glycopeptides (vancomycin and teicoplanin), linezolid, fusidic acid, tigecycline, and daptomycin were analyzed. Yearly aggregated data on the number of nonduplicate clinical MRSA and VRE isolates causing HCAI were collected.

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aureus;
Vancomycin-resistant enterococci

Results: Overall, the consumption of teicoplanin and linezolid significantly increased during the study period. A significant decrease in the incidence of HCAI-MRSA and a significant increase in the incidence of HCAI-VRE were found during the study period. A significant correlation was found between the increased use of teicoplanin and linezolid and the decreased incidence of HCAI-MRSA. By contrast, positive correlations were found between the consumption of teicoplanin and tigecycline and the incidence of HCAI-VRE.
Conclusion: This study identified various correlations between the consumption of antibiotics and the incidence of HCAI-MRSA and HCAI-VRE. Strict implementation of infection-control guidelines and reinforcement of administering appropriate antibiotic agents would be helpful in decreasing the incidence of MRSA and VRE in hospitals.

Introduction

The incidence of health-care-associated infection (HCAI) caused by multidrug-resistant bacteria has gradually risen during the last decade, especially in immunocompromised patients.[1,2] The most common causative agents of HCAI in the United States are the Gram-positive bacteria *Staphylococcus aureus* and *Enterococcus*.[3] Methicillin (oxacillin)-resistant *S. aureus* (MRSA) is of particular concern because patients with MRSA infection tend to have higher mortality rates, longer hospital stays, and higher health-care-associated costs than patients with methicillin-susceptible *S. aureus* infections.[1,4] In addition, DiazGranados et al[5] found that the mortality rate among patients with vancomycin-resistant enterococci (VREs) infection was significantly higher than that among patients with vancomycin-susceptible *Enterococcus* infections. Taiwan is no exception, and VRE and MRSA infections have become emerging infectious diseases.[6–10]

Antibiotic use is one of the risk factors for antibiotic resistance among bacterial species; however, the nature of this relationship is complicated. Although several studies have examined the relationship between antimicrobial consumption and antibiotic resistance, the findings were inconsistent, possibly due to differences in resistance profiles as well as due to differences in antibiotic-prescribing practices in different countries.[11–18] In those studies, the use of glycopeptides, extended-spectrum cephalosporins, and fluoroquinolones was demonstrated to be associated with the prevalence of MRSA and VRE.[12–18] Few studies, however, have investigated the relationship between the use of linezolid or fusidic acid and the prevalence of MRSA and VRE. In addition, the association between the consumption of tigecycline, a novel anti-Gram-positive agent derived from minocycline that has been shown to be effective against many Gram-negative rods as well as Gram-positive cocci, and the prevalence of MRSA and VRE has never been studied.[19] Similarly, no studies have so far investigated the association between the prevalence of MRSA and VRE and the consumption of daptomycin, an anti-MRSA antibiotic that has been approved by the U.S. Food and Drug Administration for the treatment of complicated skin and skin-structure infections and bacteremia due to MRSA.[20,21] In this study, we investigated the correlation between consumption of antibiotics, including vancomycin, teicoplanin, linezolid, tigecycline, fusidic acid, and daptomycin, and the incidence of HCAI-MRSA and HCAI-VRE during the period from 2000 to 2010 at a medical center in Taiwan.

Methods

Hospital setting

The National Taiwan University Hospital (NTUH) is a 2500-bed, academically affiliated medical center that provides both primary and tertiary care in northern Taiwan. The number of annual inpatient-days at the hospital increased from 624,675 in 2000 to 763,772 in 2010. Linezolid and fusidic acid were introduced into the hospital formulary in 2002. Tigecycline and daptomycin have been prescribed at the NTUH since 2007 and 2009, respectively. Some of the data analyzed in this study were included in a previous study.[16,17]

Bacterial isolates

Data on the susceptibilities of *S. aureus* to oxacillin were collected during the period from 2000 to 2010. These isolates were nonduplicate and isolates of each species from each patient recovered within 7 days were considered as a single isolate. Susceptibility testing for *S. aureus* and *Enterococcus* species followed the Clinical and Laboratory Standards Institute guidelines.[22] *S. aureus* ATCC 25923 was used as the control strain for routine disk-susceptibility testing.[22] Methicillin resistance among *S. aureus* isolates was routinely screened by measuring their growth on oxacillin (6 mg/L) in 2% NaCl-containing trypticase soy agar plate that had been incubated in ambient air at 35 °C for 24 hours.[22,23] Vancomycin resistance among *Enterococcus* species was confirmed by growth of the isolate on a brain heart infusion agar plate containing vancomycin (6 mg/L) that had been incubated in ambient air at 35 °C for 24 hours.[22]

Patients with HCAI-MRSA and HCAI-VRE

Yearly aggregated data on the number of nonduplicate clinical MRSA and VRE isolates causing HCAI were collected. HCAI was defined according to the National Nosocomial Infection Surveillance guidelines.[18] The incidence rates of HCAI-MRSA and HCAI-VRE were defined as the number of patients with HCAI-MRSA and HCAI-VRE, respectively, per 1000 inpatient-days.