Journal of Microbiology, Immunology and Infection (2016) 49, 74–82

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Effects of various antimicrobial stewardship programs on antimicrobial usage and resistance among common gram-negative bacilli causing health care-associated infections: A multicenter comparison

Chung-Chih Lai [a], Zhi-Yuan Shi [b,c], Yen-Hsu Chen [a,d,e,*], Fu-Der Wang [c,f,**]

[a] *Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan*
[b] *Division of Infectious Diseases, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan*
[c] *School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[d] *School of Medicine, Graduate Institute of Medicine, Sepsis Research Center, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*
[e] *Department of Biological Science and Technology, College of Biological Science and Technology, National Chiao Tung University, Hsinchu, Taiwan*
[f] *Division of Infectious Diseases, Department of Internal Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*

Received 21 December 2014; received in revised form 21 April 2015; accepted 21 May 2015
Available online 27 June 2015

KEYWORDS
Antibiotic consumption;
Antibiotic stewardship program;
Carbapenem;

Abstract *Background:* The effects of various antimicrobial stewardship programs (ASPs) on both antibiotic consumption and resistance among different hospitals within the same insurance system have rarely been investigated.
Methods: This 6-year retrospective study included three medical centers with similar facilities and infection control measures in Taiwan. These hospitals used different types of ASPs: one had a hospital-wide preauthorization requirement by infectious diseases physicians for all broad-spectrum antibiotics, covering all intensive care units; the second used the same

* Corresponding author. Yen-Hsu Chen, Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, 100, Tzyou 1st Road, Kaohsiung City, 807, Taiwan.
** Corresponding author. Fu-Der Wang, Division of Infectious Disease, Department of Internal Medicine, Taipei Veterans General Hospital, National Yang-Ming University of Medicine, Number 201, Section 2, Shih-Pai Road, Taipei, Taiwan.
E-mail addresses: infchen@gmail.com (Y.-H. Chen), fdwang@vghtpe.gov.tw (F.-D. Wang).

http://dx.doi.org/10.1016/j.jmii.2015.05.011

Gram-negative organisms;
Multidrug-resistant organisms

program, but excluded all intensive care units; and the third used postprescription review only. The nonsusceptibility of unduplicated isolates of gram-negative bacilli causing health care-associated infections and consumption of broad-spectrum antibiotics were analyzed.
Results: Overall, the usage of broad-spectrum antibiotics of all classes escalated significantly over time in all three hospitals, but consumption was lowest under the hospital-wide preauthorization program. Under this ASP, despite a 2-fold increase in the total broad-spectrum antibiotic consumption during study period, some declining trends of resistance were found, including ciprofloxacin-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, and carbapenem-resistant *P. aeruginosa*. By contrast, the other two hospitals with preauthorization program excluding all intensive care units and postprescription review had similar high broad-spectrum antibiotic consumption, comparable growing trends of resistant strains in general, and the correlations of antibiotic consumption and resistance were basically positive. Carbapenem-resistant *A. baumannii* increased significantly over time in all three hospitals.
Conclusion: This interhospital comparison suggested that hospital-wide preauthorization program is the most effective to reduce key gram-negative bacilli resistance, with the exception of carbapenem-resistant *A. baumannii*.

Introduction

Infections caused by multidrug-resistant organisms (MDROs) are difficult to treat, leading to significant mortality and morbidity, prolonged length of hospital stay, and excessive costs. The rise of antimicrobial resistance with a diminishing antibiotic pipeline poses a serious threat worldwide, especially concerning gram-negative microbes.[1] The overuse or misuse of antimicrobial agents is the vital component in the emergence and spread of MDROs. Antimicrobial stewardship programs (ASPs) have been advocated by many to extend the life expectancy of antimicrobial armamentarium. To date, there is growing evidence demonstrating the benefits of stewardship, including reductions of antimicrobial usage and cost.[2–4] Preprescription approval and postprescription review are two major types of ASPs. However, the long-term effects of these two ASPs have seldom been compared directly, especially across more than one institution.[3,5,6] The menace of MDRO is most serious in critically ill patients at intensive care units (ICUs), and ICUs have been the critical part for the success of ASPs. So far, few studies have been conducted to evaluate the impact of different ASPs with or without covering ICUs.

It is straightforward to predict that the more antimicrobials are used, the higher will be the resistance generated, as Darwinian selection. Many studies have been conducted to assess this association between antibiotic consumption and resistance.[7–17] However, the results have been inconsistent, and the association was not uniform among all antibiotic—organism pairs.[7–17] In addition, only a few studies compared these antimicrobial usage-versus-susceptibility relationships among different institutions simultaneously, and the effects of diverse ASPs among institutions were not surveyed.[18,19] In this study, we investigated the trends of antimicrobial resistance among key health care-associated gram-negative pathogens over a 6-year period and evaluated the relationship between resistance and broad-spectrum antibiotic usage in three medical centers, all of which were within the same insurance system but featured different ASPs.

Methods

This study was approved by the Institutional Ethics Review Boards of all participating hospitals (Kaohsiung Medical University Hospital, Taichung, Taiwan and Taipei Veterans General Hospital, Taipei, Taiwan).

Hospital settings

In this retrospective study, longitudinal multicenter database surveillance was conducted from July 2005 to December 2011. Three academically affiliated medical centers (Hospitals A, B, and C) participated in this study. Each of them has $>$ 1300 beds (the mean bed size, 1903), including $>$ 100 beds in ICUs, and they all provide both primary and tertiary care, including major surgeries, solid organ or hematopoietic stem cell transplantation, and critical care. These three hospitals are located in Taipei, Taichung, and Kaohsiung, the largest three cities in northern, central, and southern Taiwan, respectively.

These hospitals have established different strategies to promote the judicious use of antimicrobial agents long before the study period. In Hospitals A and B, preauthorization by an infectious diseases specialist is necessary to prescribe broad-spectrum antibiotics, including beta-lactam/beta-lactamase inhibitor combinations, third- and fourth-generation cephalosporins, glycopeptides, tigecycline, all carbapenems, and all fluoroquinolones. In addition to approving the antimicrobial requests, the infectious diseases specialists also offer direct interaction and feedback to prescribers at the same time. The programs are active 24 hours a day, 7 days a week. All the infectious diseases physicians, including clinical fellows, have