Journal of Microbiology, Immunology and Infection (2015) 48, 647–654

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Antimicrobial consumption and resistance in five Gram-negative bacterial species in a hospital from 2003 to 2011

Heng-Sim Lee [a,d], Yue-Xia Loh [a,d], Jen-Jain Lee [b], Chang-Shee Liu [b], Chishih Chu [c,*]

[a] *Pharmacy Division, Chiayi Branch, Taichung Veterans Hospital, Chiayi City, Taiwan, ROC*
[b] *Department of Pathology and Medical Laboratory, Chiayi Branch, Taichung Veterans Hospital, Chiayi City, Taiwan, ROC*
[c] *Department of Microbiology, Immunology, and Pharmaceuticals, National Chiayi University, Chiayi, Taiwan, ROC*

Received 19 April 2013; received in revised form 27 November 2013; accepted 15 April 2014
Available online 23 May 2014

KEYWORDS
antimicrobial agents;
carbapenem;
Gram-negative bacteria

Background: The misuse of antimicrobial agents increases drug resistance in bacteria.
Methods: The correlation between antimicrobial agent consumption and related resistance in the Gram-negative bacteria *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Proteus mirabilis* was analyzed during the period 2003–2011.
Results: Among these five bacteria, overall *E. coli* and *K. pneumoniae* were more commonly isolated from bloodstream than the other species. Regarding Enterobacteriaceae, *E. coli* and *K. pneumoniae* showed annual increases of resistance to the tested antimicrobial agents; conversely, *P. mirabilis* exhibited reduced resistance to cefuroxime, ceftriaxone and cefepime. In contrast to the relatively low antimicrobial resistance in *P. aeruginosa*, *A. baumannii* revealed high resistance, which was over 85% resistant rate to the tested antimicrobial agents and over 80% carbapenem resistance in 2011. *E. coli*, *K. pneumoniae*, and *P. mirabilis* differed in development of antimicrobial resistance after consumption of the antimicrobial agents. *K. pneumoniae* developed resistance to all antimicrobial groups, whereas resistance in *P. mirabilis* was not related to any antimicrobial consumption. *P. aeruginosa* developed resistance to β-lactam antimicrobials and aminoglycosides, whereas *A. baumanii* developed resistance to carbapenems after their use.

* Corresponding author. Department of Microbiology, Immunology, and Pharmaceuticals, National Chiayi University, 300 University Road, Chiayi 60004, Taiwan, ROC.
E-mail address: cschu@mail.ncyu.edu.tw (C. Chu).

[d] Both authors contributed equally to this paper.

http://dx.doi.org/10.1016/j.jmii.2014.04.009

Conclusion: The development of antimicrobial resistance was related to antimicrobial agents and bacterial species.

Introduction

Extended-spectrum cephalosporins, β-lactam with β-lactamase inhibitor, carbapenems, fluoroquinolones, and aminoglycosides are common antimicrobial agents used in the treatment of bacterial infections. However, application of these antimicrobial agents can induce antimicrobial resistance through mutations and the transfer of mobile elements harboring resistance genes, thus increasing the incidence of drug-resistant bacteria. Some examples include extended-spectrum β-lactamase (ESBL)-producing bacteria carrying *bla* genes for cephalosporin resistance[1,2] and fluoroquinolone-resistant bacteria with mutations in topoisomerases II and IV and altered expression of efflux pumps.[3,4]

The emergence of multidrug resistant (MDR) bacteria not only causes public health problems but also increases medical costs and the hospitalization, morbidity and mortality of patients.[5] MDR Gram-negative bacteria are major nosocomial pathogens and are increasing annually worldwide[6–11] and in Taiwan[12,13]; these species include ESBL-producing *Klebseiella pneumoniae* and *Escherichia coli*, MDR *Pseudomonas* aeruginosa,[14,15] and pan-drug resistant *Acinetobacter baumannii*.[16] Carbapenems have recently been replaced the extended-spectrum cephalosporins to treat ESBL-producing bacteria; accordingly, carbapenem resistance has been observed in *P. aeruginosa* (i.e., imipenem)[17] and *A. baumannii* (CRAB).[18,19] In Taiwan, CRAB isolates have increased gradually, with the highest in central Taiwan.[20] In this study, we analyzed the resistance profile of major Gram-negative bacteria, the consumption of antimicrobial agents and the correlation between antimicrobial usage and development of resistance.

Materials and methods

Retrospective study

All information was collected from Chiayi Branch, Taichung Veterans Hospital from 2003 to 2011. The hospital has 445 beds, including 24 beds for intensive care units, 40 beds for the respiratory care ward, 250 beds for general in-patients, and 225 beds for psychiatry patients. The hospital also has a 246-bed nursing home.

Bacterial identification and antimicrobial susceptibility test

Clinical isolates of *A. baumannii*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *P. mirabilis* were identified using the Phoenix and VITEK system in the Medical Laboratory Division. The antimicrobial susceptibility to the antimicrobial agents was determined according to the guidelines of Clinical and Laboratory Standards Institute.[21] The antimicrobial agents analyzed included: amikacin, gentamicin, and isepamicin (aminoglycosides); cefazolin, cephradine, and cephalexin (first-generation cephalosporins); flomoxef, cefuroxime, cefoxitin, ceftazidime, ceftriaxone, and cefepime (extended-spectrum cephalosporins); imipenem, meropenem, and ertapenem (carbapenems); ciprofloxacin, levofloxacin, and moxifloxacin (fluoroquinolones); ampicillin/sulbactam, amoxicillin/clavulanic acid, piperacillin, piperacillin/tazobactam (penicillins and penicillin with β-lactamase inhibitor); and tigecycline. The defined daily dose represents the antimicrobial usage of 1000 patients and was used for the statistical analysis.

Statistical analysis

Linear regression was performed to determine the correlation coefficient (r) of antimicrobial agent consumption and antimicrobial resistance of each species associated with specific years. Furthermore, correlation coefficients of antimicrobial agent consumption and antimicrobial resistance in each species were calculated, and a t test for was applied to ascertain significant differences ($p < 0.05$).

Results

Clinical isolates of five Gram-negative bacteria

The number of clinical isolates differed among the species with the highest for *P. aeruginosa*, followed by *E. coli*, *A. baumannii*, *K. pneumoniae*, and *P. mirabilis* (Table 1). Although the clinical isolates of each species differed annually, maximal number was observed for *P. aeruginosa*, *E. coli*, and *K. pneumoniae* in 2008 and for *P. mirabilis* in 2009. *A. baumannii* clinical isolates increased annually from 2003 to 2011. These five species differed in prevalence of bloodstream isolates from the highest for *E. coli* (13.5%), followed by *K. pneumoniae* (9.8%), *A. baumannii* (5.9%), *P. mirabilis* (5.9%) and *P. aeruginosa* (3.6%). Interestingly, *A. baumannii* showed an increase in bloodstream isolates and mainly were CRAB (88%).

Consumption of antimicrobial agents

The consumption level of five major antimicrobial groups differed with a gradual reduction in aminoglycosides ($r = -0.88$, $p < 0.01$) and first-generation cephalosporins ($r = -0.92$, $p < 0.01$), an annual increase in extended-spectrum cephalosporins ($r = 0.92$, $p < 0.01$) and carbapenems ($r = 0.93$, $p < 0.01$), with an exceptional use of fluoroquinolones and penicillins in 2006 and 2007,