American Journal of Infection Control ■■ (2017) ■■-■■

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Pharmacist-driven antimicrobial stewardship in intensive care units in East China: A multicenter prospective cohort study

Zhongwang Li PhD [a], Baoli Cheng PhD [a], Kai Zhang PhD [a], Guohao Xie PhD [a], Yan Wang PhD [a], Jinchao Hou PhD [a], Lihua Chu MS [a], Jialian Zhao MS [a], Zhijun Xu MS [b], Zhongqiu Lu MD [c], Huaqin Sun MD [d], Jian Zhang MS [e], Zhiyi Wang MD [f], Haiya Wu MS [g], Xiangming Fang MD [a,*]

[a] *Department of Anesthesiology and Intensive Care Unit, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China*
[b] *Intensive Care Unit, The Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China*
[c] *Emergency Intensive Care Unit, The First Affiliated Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, China*
[d] *Intensive Care Unit, The First Affiliated Hospital of Zhejiang Chinese Medicine University, Hangzhou, Zhejiang, China*
[e] *Intensive Care Unit, Hangzhou Normal University Affiliated Hospital, Hangzhou, Zhejiang, China*
[f] *Emergency Intensive Care Unit, The Second Affiliated Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, China*
[g] *Intensive Care Unit, The Second Affiliated Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, China*

Key Words:
Antimicrobial
Multidrug resistance
Intensive care unit

Background: Antimicrobial stewardship programs, particularly pharmacist-driven programs, help reduce the unnecessary use of antimicrobial agents. The objective of this study was to assess the influence of pharmacist-driven antimicrobial stewardship on antimicrobial use, multidrug resistance, and patient outcomes in adult intensive care units in China.

Method: We conducted a multicenter prospective cohort study with a sample of 577 patients. A total of 353 patients were included under a pharmacist-driven antimicrobial stewardship program, whereas the remaining 224 patients served as controls. The primary outcome was all-cause hospital mortality.

Results: The pharmacist-driven antimicrobial stewardship program had a lower hospital mortality rate compared with the nonpharmacist program (19.3% vs 29.0%; $P = .007$). Furthermore, logistic regression analysis indicated that the pharmacist-driven program independently predicted hospital mortality (odds ratio, 0.57; 95% confidence interval, 0.36-0.91; $P = .017$) after adjustment. Meanwhile, this strategy had a lower rate of multidrug resistance (23.8% vs 31.7%; $P = .037$). Moreover, the strategy optimized antimicrobial use, such as having a shorter duration of empirical antimicrobial therapy (2.7 days; interquartile range [IQR], 1.7-4.6 vs 3.0; IQR, 1.9-6.2; $P = .002$) and accumulated duration of antimicrobial treatment (4.0; IQR, 2.0-7.0 vs 5.0; IQR, 3.0-9.5; $P = .030$).

Conclusions: Pharmacist-driven antimicrobial stewardship in an intensive care unit decreased patient mortality and the emergence of multidrug resistance, and optimized antimicrobial agent use.

Global public health is severely threatened by multidrug resistance, which is due to the abuse of broad-spectrum antimicrobial agents.[1] In the United States, more than 23,000 people die from the abuse of antimicrobial agents and $20 billion is spent in related health care services.[1] To combat the resistance threat, a Presidential Executive Order outlined the promulgation of actions to expand antimicrobial stewardship programs in 2014.[2]

Antimicrobial stewardship is a multidisciplinary organizational approach that harmonizes minimal exposure and adequate coverage of antimicrobial agents.[3] The multidisciplinary team should include a pharmacist, an infectious diseases physician, a microbiologist, an information systems specialist, an infection preventionist (IP), and a hospital epidemiologist.[3] Indeed, pharmacists play a significant role in antimicrobial stewardship programs in hospitals in England.[4] As core members of antimicrobial stewardship programs, pharmacists are primarily responsible for auditing antimicrobial prescriptions and providing feedback to physicians.[3]

* Address correspondence to Xiangming Fang, MD, Department of Anesthesiology and Intensive Care Unit, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China.
E-mail address: xiangming_fang@163.com (X. Fang).

Conflicts of interest: None to report.

ZL and BC contributed equally to this work.

This study was supported by the National Key Technology Research and Development Program of China during the "12th Five-Year Plan" (2012BAI1B05).

0196-6553/
http://dx.doi.org/10.1016/j.ajic.2017.02.021

Pharmacists serve as both supervisors and directors in antimicrobial stewardship programs.[5] One single-center study reported that pharmacist-driven antimicrobial stewardship achieved a 20.1% reduction in antimicrobial agent use in the United States.[6] More recently, Adrian et al[7] reported an 18.1% reduction in antimicrobial agent consumption after implementing pharmacist-driven antimicrobial stewardship in hospitals in South Africa.

During the past decade, antimicrobial agent consumption has increased substantially in China, which has increased antimicrobial resistance that poses a serious threat to clinical practice.[8,9] Particularly in intensive care units (ICUs), the heavy use of antimicrobial agents and high rates of multidrug resistance are even more severe.[1] For instance, more than 90% of patients in ICUs receive antimicrobial therapy and more than 50% of patients are colonized or infected with multidrug-resistant strains when discharged from ICUs.[9,10] This result strongly suggests that effective antimicrobial stewardship programs are urgently needed in China.

Because of its potential role in reducing antimicrobial agent use, pharmacist-driven antimicrobial stewardship has attracted increasing attention of leaders of health care organizations in China,[11,12] and it has been introduced into some ICUs during recent years. However, to our knowledge, the effectiveness of pharmacist-driven antimicrobial stewardship in China has not been investigated. Therefore, this multicenter prospective cohort study aimed to assess the influence of pharmacist-driven antimicrobial stewardship on patient outcomes, antimicrobial use, and multidrug resistance in adult ICUs using existing resources.

METHODS

Study design and setting

This multicenter prospective observational cohort study was conducted in 8 ICUs (with approximately 160 beds) from 6 university-affiliated hospitals (with approximately 13,170 beds) in Zhejiang province during 2014. These hospitals were equipped with microbiology laboratories and monitored prescriptions of antibiotic agents and resistance patterns. All 8 ICUs had an antimicrobial stewardship program, and the ICU physicians were the leaders of these programs. All 8 ICUs implemented formulary restriction with preauthorization policies after the delivery of the official document in 2012.[11] Four ICUs implemented pharmacist-driven antimicrobial stewardship and the other 4 ICUs implemented nonpharmacist-driven antimicrobial stewardship. The average bed-to-physician and bed-to-nurse ratio in ICUs that implemented pharmacist-driven antimicrobial stewardship was similar with that of ICUs implemented with nonpharmacist antimicrobial stewardship (1.574 ± 0.159 vs 1.513 ± 0.174; $P = .871$) and (0.346 ± 0.006 vs 0.339 ± 0.010; $P = .432$), respectively. The study complied with the Declaration of Helsinki, and ethical approval was obtained from the Research Ethics Committee of the First Affiliated Hospital, School of Medicine, Zhejiang University (protocol No. 2014319).

Antimicrobial stewardship modes

Pharmacist-driven antimicrobial stewardship was implemented in 4 of the included ICUs during 2012 with the approval of hospital leadership. Pharmacists are introduced into antimicrobial stewardship programs in the ICUs on the basis of guideline recommendations and hospital resources aiming at the supervision and direction of antimicrobial agent use.[3,11] Pharmacists and physicians are trained in appropriate antimicrobial agent use and antimicrobial stewardship.[3,11,13] The following processes are audited by pharmacists: appropriate culture checking before antimicrobial therapy administration, initial administration of antimicrobial agent(s) intravenously for 72 hours, antibiotic escalation or de-escalation, identification of antimicrobial agents administered for more than 7 days, identification of antimicrobial agents administered for more than 14 days, and changing to an oral alternative. Pharmacists monitor physicians on daily rounds in the mornings from Monday-Friday and communicate immediately with physicians when inappropriate antimicrobial agents are prescribed. After that, pharmacists recommend modifications to prescriptions and the data on recommendations are recorded and reported to the antimicrobial stewardship programs. In cases in which pharmacists and physicians disagree, an infectious diseases specialist is consulted to make a final decision. In addition, pharmacists review the reports of culture results and immediately recommend antibiotic de-escalation if necessary.

By contrast, the nonpharmacist antimicrobial stewardships implemented in the other 4 ICUs did not involve any pharmacists. Physicians were trained in appropriate antimicrobial agent use and antimicrobial stewardship.[3,11,13] Moreover, physicians prescribed antimicrobial agents and reviewed prescription charts in daily practice. Physicians consulted an infectious diseases specialist to help make a decision in complex cases if necessary.

Patients

We consecutively included critically ill patients who received antimicrobial therapy within 24 hours after hospitalization in ICUs from March 1, 2014-April 30, 2014, except for patients from the ICU of the Second Affiliated Hospital of the Zhejiang University School of Medicine, who were relocated from June 1, 2014-July 30, 2014. The exclusion criteria included absence of use of antimicrobial agents during the first 24 hours in the ICU, stay in the ICU for fewer than 24 hours, age younger than 18 years, and missing data. In cases in which patients were admitted to the same ICU more than once for the same episode of illness, we only counted the first admission. All patients were assisted in either a pharmacist-driven or a nonpharmacist-driven antimicrobial stewardship program.

Definition

By definition, an infection is a pathogenic microorganism that invades sterile tissue, fluid, or body cavity, or a clinically suspected infection, and treatment involves the administration of antimicrobial agents.[14] A severe infection is defined as an infection that induces acute organ dysfunction.[14] The end point of empirical antimicrobial therapy is defined as a discontinuation of treatment based on a positive culture result or based on clinical assessment in cases of negative culture results.[3] A report delivered by the World Health Organization Collaborating Centre in 2014 established the defined daily dose as the assumed average maintenance dose of a drug that is used daily for its main indication in adults, whereas the prescribed daily dose is the average daily amount of a prescribed drug.[15] Multidrug resistance is defined as an acquired nonsusceptibility to at least 1 agent in 3 or more antimicrobial categories.[16]

Data collection

The clinical cases were identified and collected by 2 dedicated investigators who received more than 1 year of clinical training in critical care medicine and had research experience. Clinical data were collected from patients' medical records. We also obtained data from the antimicrobial agent orders reviewed, the recommendations made by pharmacists, and the accepted recommendations. The primary clinical outcome was all-cause hospital mortality. The secondary outcomes included multidrug resistance and antimicrobial agent use