International Journal of Antimicrobial Agents 48 (2016) 409–414

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Retrospective survey of the efficacy of mandatory implementation of the Essential Medicine Policy in the primary healthcare setting in China: failure to promote the rational use of antibiotics in clinics

Yonghong Xiao [a,*], Jin Wang [b], Ping Shen [a], Beiwen Zheng [a], Yingdong Zheng [c], Lanjuan Li [a,*]

[a] Collaborative Innovation Centre for Diagnosis and Treatment of Infectious Diseases, State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China
[b] Phase I Clinical Centre, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China
[c] School of Public Health, Peking University, Beijing 100191, China

ARTICLE INFO

Article history:
Received 30 December 2015
Accepted 18 June 2016

Keywords:
Essential Medicine Policy
Rational antibiotic use
Primary healthcare institutions
China

ABSTRACT

The objective of this study was to understand the impact of implementation of the Essential Medicine Policy (EMP) on the rational use of antibiotics in primary medical institutions in China. A retrospective survey was conducted in 39 primary medical institutions to compare the efficacy of EMP in rational antibiotic use. All institutions completed the survey 1 year before and 1 year after implementation of the EMP. In particular, antibiotic use and its rationality were closely examined. The institutions mainly dealt with common diseases, especially non-infectious chronic diseases. Antibiotic usage was very inappropriate both before and after EMP implementation. Before and after EMP implementation, respectively, the median outpatient cost was US$6.34 and US$5.05, 52.50% (2005/3819) and 53.41% (1865/3492) of the outpatient prescriptions contained antibiotics, and 76.23% (1132/1485) and 78.83% (1106/1403) of inpatients were administered antibiotics. In addition, 98.38% (425/432) and 97.52% (512/525) of surgical inpatients were administered antibiotics, respectively, and 80.76% (638/790) and 75.19% (503/669) of patients with a cold were prescribed antibiotics, respectively. The most commonly used antibiotics were broad-spectrum and injectable agents, including cephalosporins, fluoroquinolones and penicillins. This profile showed little change following implementation of the EMP. In conclusion, inappropriate antibiotic use is a serious problem in primary medical institutions in China. Whilst enforcing the EMP reduced the cost of medical services, it had little effect on promoting the rational use of antibiotics.

1. Introduction

Bacterial resistance has become a public health challenge worldwide, with drug-resistant bacterial infections in patients leading to high morbidity and mortality [1]. China is one of the countries with a severe bacterial resistance problem: in 2011, the prevalences of meticillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*, and carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in tertiary hospitals were 50.5%, 71.2%, 23.4% and 56.8%, respectively [2]. Furthermore, in non-central city hospitals in 2011, the prevalences of ESBL-producing *E. coli*, macrolide-resistant *Streptococcus pneumoniae* and quinolone-resistant *E. coli* were as high as 64.8%, 97.1% and 57.4%, respectively [3]. Moreover, 17.4%, 25.0%, 71.2% and 44.4% of the healthy population in Nanjing carry MRSA, ESBL-producing *Klebsiella pneumoniae*, erythromycin-resistant *S. pneumoniae* and sulfamethoxazole-resistant *Haemophilus influenzae*, respectively, in their nasopharynx [4]. If this problem is not tackled urgently, it may lead to the disastrous situation where humankind eventually lacks effective drugs against bacterial infections. This is emphasised by the warning issued by the World Health Organization (WHO) in 2011, which stated 'combat drug resistance: no action today, no cure tomorrow' [1,5,6].

Use of antibiotics and the occurrence of bacterial resistance are closely associated. In particular, inappropriate use of antibiotics (e.g. excessive prescription and unregulated use) promotes the occurrence and spread of resistant micro-organisms [7]. In the last 10 years, Chinese regulatory agencies imposed a number of measures, which were implemented in a stepwise fashion, to regulate the use of antibiotics in general hospitals [8]. These measures successfully reduced antibiotic sales and the frequency of

* Corresponding author. Collaborative Innovation Centre for Diagnosis and Treatment of Infectious Diseases, State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China. Fax: 86-571087236421.
E-mail addresses: xiao-yonghong@163.com (Y. Xiao); ljli@zju.edu.cn (L. Li).

http://dx.doi.org/10.1016/j.ijantimicag.2016.06.017
0924-8579/

antibiotic-containing prescriptions in general hospitals in China. However, those measures had less involvement with the primary medical institutions of China (Chinese medical service institutions consist of three-level hospitals: primary clinical service such as described in the investigation, secondary hospitals and tertiary hospitals). These institutions provide basic healthcare services to most of the population: the National Health and Family Planning Commission of China showed that in 2012, 6.888 billion patient visits occurred nationally, of which 4.109 billion (59.65%) occurred in primary medical institutions [9]. However, these institutions tend to be relatively poorly managed and their staff less well trained than those in general hospitals. These factors mean that inappropriate use of antibiotics is more prominent in these institutions and this is likely to have a large impact on the development of bacterial resistance in China [10].

To promote rational antibiotic use, the WHO has developed a serial of strategies, including the Essential Medicine Policy (EMP), and implementation of the EMP has been shown to have had a positive effect in several countries [11–13]. Development of a National Essential Drugs List (NEDL) is the core component of the EMP. The NEDL was developed in China in 1982 for the first time but without implementation. Therefore, in 2009 the government disseminated the primary institution version of the NEDL and launched a series of actions to ensure implementation of the EMP in primary healthcare institutions following the initiation of a new round of healthcare reform [14]. To understand the impact of the EMP on the rational use of antibiotics in China, this retrospective investigation was conducted. Antibiotic usage before and after implementation of the EMP in representative urban and rural primary medical institutions in China was compared.

2. Materials and methods

2.1. Participants

Representative primary medical institutions in China that had implemented the EMP and were located in various regions with differing levels of socioeconomic development were selected for this survey. Specifically, there were 24 rural township health centres (RTHCs) from two underdeveloped inland provinces (Jilin and Henan; four RTHCs each), three developed coastal provinces (Shandong, Jiangsu and Zhejiang; four RTHCs each) and the city of Beijing (four RTHCs). There were also 24 city community health service centres (CCHSCs), 2 in each provincial capital city, 2 in a non-capital city in each province and 4 in Beijing.

2.2. Randomisation and sample size

This was a retrospective investigation. The records of each participating institution 1 year before and 1 year after EMP implementation were randomly sampled and analysed. The study period was either 2009–2010 or 2010–2011, depending on the date that the NEDL (primary institution version) was disseminated in each region. For both study years, in every primary healthcare institution the patient records of 50 outpatients and 50 inpatients (both surgical and non-surgical inpatients) from 2 months in each year (1 month in the spring and 1 month in the fall) were selected randomly. Occasionally, there were fewer than 50 inpatients for a particular sample month and in this case all inpatients were included in the investigation.

2.3. Data collection

The general nature of each institution (including its size, number and type of staff, financial status and the services provided to patients) and the drug and antibiotic usage by outpatients and inpatients were investigated. Use of antibiotics for common diseases was also investigated. Antibiotics were classified according to the Anatomical Therapeutic Chemical (ATC) classification system recommended by the WHO. The main indicators of the WHO regarding drug use in medical institutions were assessed, including the average number of drugs prescribed per outpatient visit, the proportion of prescriptions that contained antibiotics, the appropriateness of antibiotic use, the category of antibiotics and the cost per visit [15,16]. Specifically, use of antibiotics in outpatients with a cold, pharyngitis, acute bronchitis and urinary tract infections (UTIs) were investigated. The rates, categories and appropriateness of antibiotic use in inpatients, their medical costs and the prophylactic use of antibiotics in surgical patients were also investigated.

According to the standards of the 'Principles of clinical use of antibiotics', which follow international guidelines [17] and were issued by the Chinese Ministry of Health in 2004 [18], an antibiotic prescription was considered to be proper (i.e. the correct decision had been made by the prescriber) if it followed the standard treatment regimen and duration that was indicated for the patient's clinical infection or prophylaxis. Antibiotic use was considered to be partially proper when the clinical condition of the patient justified the prescription of antibiotics for treatment or prophylaxis but the treatment regimen (incorrect choice) or its duration (incorrect use) was incorrect. Antibiotic use was considered improper when the clinical condition of the patient did not justify antibiotics for either treatment or prophylaxis (incorrect decision and data insufficient).

To ensure data quality, investigators underwent standard training in advance and two investigators were assigned to each medical institution. One investigator completed the investigational form and the other conducted the review. After the research co-ordinating centre received the raw data, the centre audited and verified the authenticity and logicality of the data. The quality-controlled data were then analysed.

2.4. Data analysis and statistics

Data entry was performed using the double-entry method. Once the entry was completed and verified, the database was locked. SPSS Statistics for Windows v.20.0 (IBM Corp., Armonk, NY) was used for data analysis. The medical expenses incurred by the patients, the drug cost, and the usage and appropriateness of antibiotics in inpatients and outpatients before and after implementation of the EMP were assessed. Continuous variables were expressed as the range, median and mean, and categorical data were expressed as percentages. Sales and income were converted from the Chinese currency into US dollars using an exchange rate of 6.62 Chinese Yuan to US$1.

3. Results

A total of 48 primary medical institutions participated in this study, of which 9 were excluded from the analysis (6 because the original data were incomplete and 3 because their data failed the quality control audits, i.e. >50% of the patient records in an institution failed quality control). Thus, 39 primary medical institutions were included in the analysis, of which 8, 6, 4, 7, 8 and 6 were from Jilin, Henan, Shandong, Jiangsu, Zhejiang and Beijing, respectively. Of the 39 institutions, 23 were CCHSCs and 16 were RTHCs; 15 lacked an inpatient unit. In total, 7800 outpatient records were collected from the 39 institutions, from which 7311 passed quality control processes. Of these, 5453 records were from CCHSCs and 1858 records were from RTHCs. Furthermore, 3819 and 3492 records were from before and after the EMP implementation, respectively. There were 2888 quality-controlled inpatient records, of which 957 were surgical patients and 1931 were non-surgical patients. Of the 2888