Journal of Global Antimicrobial Resistance 19 (2019) 201–206

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

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

Evaluation of antibacterial use in outpatients of township and community primary medical institutions in a district of Sichuan Province, China

Qian Zhan[a], Y.L. Wang[b,*], Xi Chen[c]

[a] Department of Pharmacy, Mianyang People's Hospital, Mianyang, Sichuan, China
[b] Hepatobiliary Surgery, Mianyang People's Hospital, Mianyang, Sichuan, China
[c] Department of Pharmacy, Mianyang Orthopedic Hospital, Mianyang, Sichuan, China

ARTICLE INFO

Article history:
Received 31 July 2018
Received in revised form 25 April 2019
Accepted 30 April 2019
Available online 8 May 2019

Keywords:
Outpatient prescription
Antibacterial
Township health centre
Community health service centre
Primary health care

ABSTRACT

Objectives: Antibacterial use in township health centres (THCs) and community health service centres (CHSCs) in a district of Sichuan Province, China, was investigated. By analysis of the common irrational use of antibacterials in such primary medical institutions, the purpose of promoting rational use of antibacterials can be achieved.

Methods: Outpatient prescriptions were randomly selected from 12 THCs and 5 CHSCs in a district of Sichuan Province from July–September 2015 and antibacterial use in these outpatient prescriptions was investigated.

Results: The average usage rate of antibacterials in outpatient prescriptions of THCs and CHSCs was 61.05% and 35.07%, respectively, and the average proportion of rational antibacterials in prescriptions was 59.88% and 77.07%, respectively. In THCs, there was an extremely significant difference between centre A and centre N, especially for two antibacterial indicators (irrational antibacterials and irrational drug frequency). There was also an extremely significant difference between centre P and centre T, especially for the same two abovementioned indicators. These results were evaluated in relation to the implementation of quality control management of rational drug use.

Conclusion: There are many irrational problems in antibacterial use in outpatient prescriptions of THCs and CHSCs in China. Therefore, it is necessary to strengthen the training and management of antibacterial use at primary medical institutions, and grassroots pharmacists should also play an active role in antibacterial drug management.

1. Introduction

As a result of abuse of antibacterials, the trend of antimicrobial resistance in bacteria is becoming more and more serious. Discovery of new antibacterials takes a long time and costs a huge amount of money, and the rate of research and development has not kept pace with the development of drug-resistant bacteria. Therefore, rational antibacterial use has become a matter of great concern for public health in various countries around the world in order to curb antimicrobial resistance.

In China, township health centres (THCs) and community health service centres (CHSCs), both providing public welfare support, are primary-level healthcare facilities and are the core foundation of the health system. THCs, which are comprehensive medical organisations established in villages and townships, are responsible for preventive health care, basic medical services and rural public-health management of farmers. As a non-profit organisation, in principle, only one government-sponsored THC was set up in each township. CHSCs refer to primary healthcare institutions that provide residents in certain urban communities with healthcare activities, including health education, prevention, health care, rehabilitation, family planning services and treatment of general common diseases. Therefore, THCs and CHSCs are important links in actively curbing bacterial drug resistance.

At the end of 2015, a special inspection for antibacterial use in outpatient prescriptions in a district of Sichuan Province, China, was conducted. Antibacterial use in outpatient prescriptions was investigated and analysed to provide a reference for future quality control work for rational antibacterial use.

* Corresponding author.
E-mail address: wangyulong2018@126.com (Y.L. Wang).

https://doi.org/10.1016/j.jgar.2019.04.021
2213-7165/

2. Methods

2.1. Study aim

The special inspection for antibacterial use in outpatient prescriptions included all 12 THCs and 5 CHSCs under the jurisdiction of a district health and family planning commission in Mianyang City, Sichuan Province.

2.2. Investigation method

From July–September 2015, 150 outpatient prescriptions were randomly selected from each THC and CHSC. The prescription extraction method referred to the sampling method of the '*National technical program for monitoring clinical application of antibacterials*' [1] as follows.

First, the first sample prescription was determined. One Ren Min Bi was randomly selected and the first digit of its serial code was used as the number of the first sample prescription.

Second, the sample interval number was confirmed. All outpatient prescriptions from July–September 2015 were collected and the total number of prescriptions was divided by 150, and the integer of the result was the sampling interval, e.g. if the total number of prescriptions is 980, then 980/150 = 6.53, thus an outpatient prescription was selected as a survey sample for every 6 prescriptions. In this regard, through the above two steps, 150 prescriptions were confirmed.

Third, because of the inability to evaluate rational use of antibacterials, prescriptions with no diagnosis or with a vague diagnosis, such as prescribing or physical examinations, were excluded. The remaining prescriptions were called effective prescriptions.

2.3. Appraisal method of rational drug use

Special comments on antibacterial use in outpatient prescriptions were based on the following relevant guidelines or regulatory documents: '*Guidelines on clinical application of antibacterials (2015 version)*', '*National guidelines on antibacterial therapy (2012 version)*', '*Chinese National Formulary*', '*Hospital prescription comment management standard (trial version)*', '*Prescription management measures (2007)*', '*Internal medicine (8th edition)*', *etc.* The guidelines listed above are all in Chinese and are all at national level.

To reduce errors in the judgement of rational drug use, pharmacy experts were divided into two groups. Each outpatient prescription was judged by the two groups in order to determine rationality, and a final consensus was reached.

This survey mainly examined two indicators of antibacterial use: (i) the usage rate of antibacterials in outpatient prescriptions; and (ii) the proportion of rational antibacterials in outpatient prescriptions. The former indicator equals the percentage of the number of outpatient prescriptions with antibacterials divided by the number of effective prescriptions, and the latter equals the percentage of the cumulative number of rational prescriptions divided by the number of effective prescriptions.

2.4. Statistical analysis

Microsoft Excel 2013 (Microsoft Corp., Redmond, WA, USA) was used to collate the prescribing information data of the THCs and CHSCs. SPSS Statistics v.17.0 (SPSS Inc., Chicago, IL, USA) was used to perform the χ^2 test on the relevant indicators of antibacterial use.

3. Results

3.1. Antibacterial drug indicators of outpatient prescriptions

The two expert groups made a judgement on the rationality of antibacterial use in outpatient prescriptions. The two antibacterial indicators in each health centre, namely the usage rate of antibacterials in outpatient prescriptions and the proportion of rational antibacterials in outpatient prescriptions, were calculated (Tables 1 and 2).

The average usage rate of antibacterials in outpatient prescriptions in THCs and CHSCs was 61.05% and 35.07%, respectively, and the average proportion of rational antibacterials was 59.88% and 77.07%, respectively.

In the 12 THCs, centre A had the lowest usage rate of antibacterials in prescriptions (30.00%) and the highest proportion of rational antibacterials in prescriptions (86.67%). Centre N had the highest usage rate of antibacterials in prescriptions (94.33%) and the lowest proportion of rational antibacterials in prescriptions (32.62%). A χ^2 test was conducted on the usage rate of antibacterials in prescriptions between centres A and N (30.00% vs. 94.33%; $P < 0.001$). Furthermore, a χ^2 test was conducted on the proportion of rational antibacterials in prescriptions between centres A and N (86.67% vs. 32.62%; $P < 0.001$).

In the 5 CHSCs, centre P had the lowest usage rate of antibacterials in prescriptions (21.33%) and its proportion of rational antibacterials in prescriptions was highest (88.00%). Centre T had the highest usage rate of antibacterials in prescriptions (50.00%) and the lowest proportion of rational antibacterials in prescriptions (60.00%). Following the same method as above, a χ^2 test was conducted between centres P

Table 1
Antibacterial drug indicators of outpatient prescriptions in township health centres (THCs) in a district of Sichuan Province, China.

THC	No. of effective prescriptions	No. of antibacterial prescriptions	Usage rate of antibacterials in prescriptions (%)	No. of rational prescriptions	Proportion of rational antibacterials in prescriptions (%)
A	150	45	30.00	130	86.67
B	147	78	53.06	121	82.31
C	149	68	45.64	120	80.54
D	125	62	49.60	83	66.40
E	149	67	44.97	95	63.76
F	150	79	52.67	92	61.33
G	150	120	80.00	79	52.67
H	141	98	69.50	74	52.48
J	140	89	63.57	70	50.00
K	148	98	66.22	67	45.27
M	130	113	86.92	53	40.77
N	141	133	94.33	46	32.62
Total	1720	1050	61.05	1030	59.88

Table 2
Antibacterial drug indicators of outpatient prescriptions in community health service centres (CHSCs) in a district of Sichuan Province, China.

CHSC	No. of effective prescriptions	No. of antibacterial prescriptions	Usage rate of antibacterials in prescriptions (%)	No. of rational prescriptions	Proportion of rational antibacterials in prescriptions (%)
P	150	32	21.33	132	88.00
Q	150	33	22.00	129	86.00
R	150	51	34.00	128	85.33
S	150	72	48.00	99	66.00
T	150	75	50.00	90	60.00
Total	750	263	35.07	578	77.07

and N on the usage rate of antibacterials in prescriptions (21.33% vs. 50.00%; $P < 0.001$) and on the proportion of rational antibacterials in prescriptions (88.00% vs. 60.00%; $P < 0.001$).

We believe that these statistical results are closely related to the quality control of rational drug use in different township or community primary medical institutions.

3.2. Distribution of irrational drug use in outpatient prescriptions

As the vast majority of THCs and CHSCs had already implemented electronic prescriptions, there were very few non-standard-writing prescriptions. Therefore, non-standard-writing prescriptions were disposed by the way of communication and feedbacked to the doctor. The non-standard-writing problem was not included in the distribution statistics of irrational drug use.

The distribution of irrational antibacterial use in outpatient prescriptions for THCs and CHSCs is shown in Tables 3 and 4, respectively. The data indicate that most irrational problems in THCs were irrational drug frequency (44.28%), irrational antibacterials (24.62%) and non-indication drug use (13.99%). Most irrational problems in CHSCs were irrational drug frequency (36.99%), irrational antibacterials (31.66%) and irrational drug dosage (12.23%).

3.3. Distribution of drug categories with irrational problems in outpatient prescriptions

The distribution of drug categories with irrational problems in outpatient prescriptions for THCs and CHSCs is shown in Tables 5 and 6, respectively. In the process of statistical analysis, the drug categories involved were counted once for irrational drug combinations. For example, when levofloxacin was combined with azithromycin, quinolones or macrolides, they were counted once respectively. As another example, when cefazolin was combined with cefotaxime, cephalosporins were counted twice.

The top three drug categories with irrational drug use in THCs were cephalosporins (70.69%), penicillins (9.62%) and quinolones (7.74%). The top three drug categories with irrational drug use in CHSCs were cephalosporins (34.93%), nitroimidazoles (26.20%) and penicillins (14.93%). The difference in category distribution was closely related to the drug use rate. In township and community primary medical institutions, cephalosporins, penicillins, nitroimidazoles and quinolones are commonly used drugs.

4. Discussion

4.1. Analysis of the main problems in irrational drug use

Through this special inspection of antibacterials, we found that there were mainly seven irrational problems of antibacterial use in THCs and CHSCs.

4.1.1. Non-standard diagnosis

A non-standard diagnosis mainly means that the diagnosis is not clear, e.g. in a diagnosis of gastritis, it is not clear whether it is chronic or acute. As another example, in post-operative abortion it was not clear whether this was for prevention or treatment of infection. There was little information in outpatient prescriptions, and the principle of anti-infective treatment for different diagnoses was different. Therefore, non-standard diagnoses often influence the judgement of the rationality of drug use.

4.1.2. Irrational antibacterials

Irrational antibacterials mainly means that the wrong antibacterial drug was selected for anti-infective treatment according to the diagnosis on the prescription. For example, if acute tonsillitis was treated with cefoperazone/sulbactam, an enzyme inhibitor

Table 3
Distribution of irrational antibacterial use in prescriptions of township health centres (THCs) in a district of Sichuan Province, China.

THC	Non-standard diagnosis	Irrational antibacterials	Irrational combination	Non-indication drug use	Irrational drug frequency	Irrational drug dosage	Irrational administration route	Total of questions in centre
A	4	3	1	0	8	6	0	22
B	2	10	4	8	0	0	2	26
C	2	18	0	5	3	4	0	32
D	0	15	1	3	19	8	0	46
E	1	23	7	10	31	4	2	78
F	5	19	0	15	38	8	1	86
G	6	19	0`	18	52	8	0	103
H	3	17	3	17	44	3	0	87
J	2	20	13	7	29	14	1	86
K	1	8	0	6	76	7	0	98
M	4	12	3	19	53	3	0	94
N	2	49	7	13	30	1	5	107
Total of different questions	32	213	39	121	383	66	11	865
Composition ratio of different questions	3.70%	24.62%	4.51%	13.99%	44.28%	7.63%	1.27%	100%

Table 4
Distribution of irrational antibacterial use in prescriptions of community health service centres (CHSCs) in a district of Sichuan Province, China.

CHSC	Non-standard diagnosis	Irrational antibacterials	Irrational combination	Non-indication drug use	Irrational drug frequency	Irrational drug dosage	Irrational administration route	Total of questions in centre
P	4	3	0	0	7	3	4	21
Q	0	13	1	4	10	2	0	30
R	0	22	2	4	29	12	0	69
S	0	29	3	8	27	7	0	74
T	0	34	31	0	45	15	0	125
Total of different questions	4	101	37	16	118	39	4	319
Composition ratio of different questions	1.25%	31.66%	11.60%	5.02%	36.99%	12.23%	1.25%	100%

Table 5
Distribution of drug categories with irrational problems in township health centres (THCs) in a district of Sichuan Province, China.

THC	Penicillins	Cephalosporins	Quinolones	Macrolactones	Clindamycin	Nitroimidazoles	Aminoglycosides	Antifungals	Total count of drug categories with irrational problems in centre
A	1	15	3	3	1	0	0	0	23
B	5	11	6	0	2	3	2	1	30
C	6	23	0	2	0	1	0	0	32
D	3	34	2	3	0	5	0	0	47
E	1	70	5	3	2	4	0	0	85
F	9	63	5	0	6	3	0	0	86
G	2	90	5	3	3	0	0	0	103
H	3	63	12	1	2	3	6	0	90
J	3	63	12	12	7	0	0	2	99
K	12	69	8	5	0	4	0	0	98
M	11	72	7	3	0	2	2	0	97
N	31	66	5	10	1	0	0	1	114
Total count of drug category	87	639	70	45	24	25	10	4	904
Composition ratio of different drug categories	9.62%	70.69%	7.74%	4.98%	2.65%	2.77%	1.11%	0.44%	100%

Table 6
Distribution of drug categories with irrational problems in community health service centres (CHSCs) in a district of Sichuan Province, China.

CHSC	Penicillins	Cephalosporins	Quinolones	Macrolactones	Clindamycin	Nitroimidazoles	Aminoglycosides	Antifungals	Total count of drug categories with irrational problems in centre
P	2	9	3	0	0	7	0	0	21
Q	1	14	0	0	8	7	1	0	31
R	4	43	4	1	10	6	2	1	71
S	22	35	4	0	8	8	0	0	77
T	24	23	12	28	0	65	3	0	155
Total count of drug category	53	124	23	29	26	93	6	1	355
Composition ratio of different drug categories	14.93%	34.93%	6.48%	8.17%	7.32%	26.20%	1.69%	0.28%	100%

compound, there is a problem of the wrong drug selection. In general, the broad-spectrum enzyme inhibitor compound is mainly aimed at resistant bacteria and is not recommended for outpatients. Another example is trichomonas vaginitis treated by oral administration of levofloxacin tablets, as according to relevant guidelines, nitroimidazoles are recommended [2].

4.1.3. Irrational combination

Irrational combination mainly refers to a drug combination without indication or a drug combination with incompatibility, or that the drug combination cannot achieve synergistic effects, e.g. it is irrational for acute bronchitis to be treated with oral levofloxacin tablets and oral azithromycin capsules as, on the one hand the two drugs may both cause prolonged QT interval and other cardiovascular side effects and, on the other hand, with regard to the common pathogens of acute bronchitis levofloxacin can basically cover the antibiogram of azithromycin and so one of them alone can meet the treatment requirements.

4.1.4. Non-indication drug use

Non-indication drug use mainly refers to the fact that there was no indication for using antibacterials according to the prescription

diagnosis. For example, patients with rheumatoid arthritis were treated with clindamycin hydrochloride capsules orally. As another example, patients with rectal cancer were administered cefoperazone/sulbactam. According to *Internal medicine (8th ed)* [3], the above anti-infective treatments are unreasonable and represented this kind of problem.

4.1.5. Irrational drug frequency

Irrational drug frequency mainly means that according to the drug instruction or the '*Chinese National Formulary*', the frequency of drug use is irrational. For example, the recommended use of cefradine capsules is 0.25–0.5 g four times a day orally, but in fact all of the oral dosage forms of cefradine in the inspection were 0.5 g three times a day. As another example, the correct use of cefotaxime sodium injection is administration every 12, 8 or 6 h, but the usage of some prescriptions in the inspection was once per day. Since cephalosporins are time-dependent antibacterials with a short half-life and a short post-antibiotic effect, multiple daily doses are required to achieve a better anti-infective effect [4]. However, ceftriaxone can be administered one daily owing to its long half-life.

4.1.6. Irrational drug dosage

An irrational drug dosage mainly means that the daily dose of the antibacterial is lower than the minimum or higher than the maximum instructional daily dose, especially for children, according to the standard daily dose reference, the '*Chinese National Formulary*'. For example, cefaclor granules were prescribed at 0.25 g three times a day orally for a child 6 months of age, which is the adult daily dose. If the antibacterial daily dose is excessively high, toxicity and side effects of the drug can result, even sometimes unnecessary drug-induced injury to patients can occur. On the other hand, a low daily dose can result in a poor anti-infective effect and can even induce drug resistance.

4.1.7. Irrational administration route

In this inspection, an irrational administration route mainly included oral dosage forms for vaginal use or injection forms for topical use or flushing. For example, metronidazole tablets cannot be prescribed for vaginal use. The safety and efficacy of vaginal use of metronidazole tablets has not been fully assessed. Moreover, because of the different environment of vaginal and gastrointestinal fluids, metronidazole oral tablets will not be fully released in the vagina and the drug efficacy will be greatly reduced. As another example, metronidazole injection cannot be used for trauma washing. Because the local skin tissue has poor transdermal absorption of metronidazole, it is difficult for the drug to reach an effective tissue concentration. At the same time, a drug with a high concentration on the skin surface has an advantage in screening pathogenic bacteria to induce the occurrence of drug resistance.

4.2. Summary

In this special inspection of antibacterials in outpatient prescriptions, antibacterial indicators for several THCs and CHSCs conformed to or were in close agreement with the relevant regulations of the National Health Commission of the People's Republic of China. However, we still regretted to find that there were many irrational problems in the actual use of antibacterials in most township and community primary medical institutions. For this issue, we have the following suggestions.

First of all, in medical institutions, the medical quality management department of the hospital should unite with relevant professional departments, strengthen the supervision of the rational use of antibacterials, and strengthen the relevant professional training for clinical medical staff.

Second, pharmacists should also actively play an important role in the management of rational drug use. On the one hand, through prescription comments, pharmacists can strictly enforce the implementation of relevant guidelines or regulatory documents, especially drug instructions and the '*Chinese National Formulary*'. And in the process of dispensing prescriptions, pharmacists should refuse apparently irrational prescriptions. This is one of the duties that pharmacists must perform. On the other hand, pharmacists should also take advantage of their own professional knowledge and actively devote themselves to the management of rational drug use in primary medical institutions, which cannot only improve pharmacists' professional quality but also greatly benefit the standardised management of rational drug use.

Third, in addition, the health administrative departments at all levels should play active roles in the local Quality Control Center of Pharmaceutical Affairs, leading and supervising the implementation of rational drug management for antibacterials at various localities. According to China's national conditions, active intervention of the health administrative department can often play an important role from the administrative level.

Fourth, it is also necessary for primary medical institutions to strengthen drug promotion work and to increase public awareness of antibacterials.

Fifth, in particular, bacterial resistance surveillance is usually not carried out in primary medical institutions, mainly for the following reasons. In township and community primary medical institutions in China, the patient's condition is usually straightforward. A patient with a relatively complex condition will be referred to a higher level medical institution. Moreover, there is a lack of hardware for microbiology laboratories in township and community primary medical institutions. Finally, the general education level of patients in primary medical institutions is not high, and patients often complain about troubles and cost problems. For these reasons, pathogen inspection is rarely done in hospital outpatient clinics in primary medical institutions. In fact, such problems are also common in outpatient clinics throughout the world [5].

Finally, the survey was conducted at the end of 2015, but this article truly reflects the inspection. There are currently few published articles in the English literature on the use of antimicrobials in township and community primary medical institutions in China. Therefore, we have written this article as a reference. Through special rectification work over 3 years (2011–2013), there has been significant progress in the rational use of antibacterials in China. However, through our grassroots research, it is found that the management of antibacterials in primary medical institutions requires further strengthening. This is also the significance of the true publication of this paper.

Funding

None.

Competing interests

None declared.

Ethical approval

Not required.

Acknowledgments

The authors thank all of the colleagues and leaders, notably of the District Health Commission and the District Quality Control Center of Pharmaceutical Affairs.

References

[1] Chinese Center for Antibacterial Surveillance. National technical program for monitoring clinical application of antibacterials. Beijing, China: Chinese Center for Antibacterial Surveillance. https://wenku.baidu.com/view/5589fe881711cc7930b71694.html. [Accessed 22 March 2017].
[2] Nanshan Z, Xirun W, Xiaojun M, Chen W, Rui W, Dayou W, et al. Guidelines on clinical application of antibacterials (2015 version). Beijing, China: National Health and Family Planning Commission of the People's Republic of China; 2015. . . [Accessed 20 March 2017] http://www.moh.gov.cn.
[3] Fang Jinyuan. Colorectal cancer. In: Junbo G, Yongjian X, editors. Internal medicine. 8th ed. Beijing, China: People's Health Publishing House; 2014. p. 394–400.
[4] MacKenzie FM, Gould IM. The post-antibiotic effect. J Antimicrob Chemother 1993;32:519–37.
[5] Hayward GN, Moore A, Mckelvie S, Lasserson DS, Croxson C. Antibiotic prescribing for the older adult: beliefs and practices in primary care. J Antimicrob Chemother 2019;74:791–7.