Author's response to reviews

Title: An outpatient antibiotic stewardship intervention during the journey to JCI accreditation

Authors:

Ping Song (spfcckc@126.com)
Wei Li (liwei660501@yahoo.com)
Quan Zhou (zhouquan142602@zju.edu.cn)

Version: 4 Date: 28 December 2013

Author's response to reviews:

Dear Dr Catherine MT Sherwin
Associate Editor
BMC Pharmacology and Toxicology

Thank you very much for giving us the second opportunity of manuscript revision. The comments from reviewers are very pertinent. We thank them for their professional work and encouragements to us. Response to the comments and revised points are as follows.

Our response to Referee 2

Referee 2 EVALUATION

1. Conducting more literature review in order to establish make clear statements on problem magnitude and to convince about the rationale and importance of this study. I cannot find the evidence e.g. number or figures to support the serious threat due to AMR. This is just one among other points that the authors need to work more on this issue.

Author response:

Dr. Nithima Sumpradit gave us very good suggestions toward the background section. We have revised this section. Three references were added. More clear statements on problem magnitude were made. We believe the readers will understand the rationale and importance of this study by reading the background. Sentences were polished in order to introduce why we did this study more naturally and more logistically.

More descriptions on antimicrobial resistance (AMR) were made. Evidence to support the serious threat due to AMR has been presented.

------paragraph 1

Over use or the improper use of antibiotics can result in drug resistant bacteria as well as considerable expense to health care system [1]. According to a new report “Antibiotic Resistance Threats in the United States, 2013” issued by the U.S. Centers for Disease Control and Prevention (CDC), antibiotic resistance in
the United States adds $20 billion in excess direct health care costs, with additional costs to society for lost productivity as high as $35 billion a year. The use of antibiotics is the single most important factor leading to antibiotic resistance. Up to 50 percent of all the antibiotics prescribed for people are not needed or are not prescribed appropriately [2].

It is imperative to create a culture of safety and quality within an organization that strives to continually improve the quality of antibiotic prescribing. A systematic review showed that antibiotic prescribing is a complex process influenced by factors affecting all the actors involved, including physicians, other healthcare providers, healthcare system, patients and the general public [3]. Sumpradit et al reported that prescription behavior could be influenced by the factors like knowledge, attitudes, subjective norms, peer pressure, patient expectations, drug promotion, physician’s diagnostic skill and exposure to hospital formularies and standard therapeutic guidelines [4].

A search of Medline between January 1 1993 and October 31 2013 revealed only two intervention studies when using the keywords: “antimicrobial stewardship and intervention and outpatient and prescribing”. One study evaluated the effect of clinician education coupled with audit and feedback on broad-spectrum antibacterial prescribing for pediatric outpatients with acute respiratory infections [11], and the other study assessed the effect of a computerized clinical decision support system (CDSS) on preventing misuse of fluoroquinolone and azithromycin for acute respiratory infections [12]. Compared with these interventions confined to special type of infection or particular class of antibiotics, multifaceted interventions for quality improvement in outpatient antibiotic prescribing has not been reported.

According to reviewer 2’s suggestions, we added some contents. “Rational antibacterial use was listed as one of the nine patient safety goals in SAHZU in 2012-2013. A working group composed of infectious disease physicians, pharmacists, microbiologists, and administrators was established. This group sought to implement multifaceted interventions at the individual, organizational and policy levels to change antibacterial prescription practices [4]. During the journey to JCI accreditation, the SAHZU group performed an outpatient antibacterial stewardship intervention. The aim of this article was to discuss the effectiveness of such stewardship intervention in the outpatient setting and provide some reference for international counterparts.”

Referee 2 EVALUATION ----
2. Seeking extensive editorial assistance to be able to articulate ideas, strengthen arguments and comply with academic writing structure. For example, the first statement in the first paragraph says that AMR is a major global threat for two decades. Theoretically, the next sentence should clarify this point. It should not have introduced a new idea (i.e., Sumpradit et al....) at this point.
Author response:
We have revised according to reviewer 1’ suggestions. We paid more attention to academic writing structure.

Referee 2 EVALUATION ----
3. Ensuring all details are properly addressed. One example among many others is Table 1 - what do the levels 1, 2 and 3 in the Table stand for? Does it represent 'first-line,' 'second-line' and 'third-line' on page 6? If so, should it be noted somewhere for this clarification?

Author response:
We have noted in the table 1 according to reviewer 1’ suggestion. ------“Level 1: non-restricted (also called “first line”) antibacterials; Level 2: restricted (“second line”) antibacterials; Level 3: special-grade (“third line”) antibacterials”.

Our response to Referee 1
Referee 1 EVALUATION
General:
Please see the attached tracked-changes version of the manuscript for wording suggestions. Further grammatical modifications may be needed prior to publication.

Author response:
Thanks very much for Joshua Courter’s generous polishing work toward our manuscript. Very professional polishing! We can imagine what a dedicated person he is. We have revised the relevant part strictly according to reviewer 1’ suggestions. Also, grammatical modifications have been made to the best of our ability.

Referee 1 EVALUATION
Major Compulsory Revisions:
In general, see language edits throughout the attached document

Author response:
We have revised the relevant part according to reviewer 1’ suggestions. Thanks very much for Joshua Courter’s generous polishing work toward our manuscript.

Referee 1 EVALUATION
Major Compulsory Revisions:
Page 4; Paragraph 2; Sentence 4: Would recommend changing wording to reflect that a search of Medline was performed, and list the keywords.

Author response:
We have revised the relevant part according to reviewer 1’ suggestions. -------- A search of Medline between January 1 1993 and October 31 2013 revealed only two intervention studies when using the keywords: “antimicrobial stewardship and intervention and outpatient and prescribing”. One study evaluated the effect
of clinician education coupled with audit and feedback on broad-spectrum antibacterial prescribing for pediatric outpatients with acute respiratory infections [11], and the other study assessed the effect of a computerized clinical decision support system (CDSS) on preventing misuse of fluoroquinolone and azithromycin for acute respiratory infections [12]. Compared with these interventions confined to special type of infection or particular class of antibiotics, multifaceted interventions for quality improvement in outpatient antibiotic prescribing has not been reported.

Referee 1 EVALUATION

Major Compulsory Revisions:

Page 8; Results; Paragraph 1: Need to list monetary units for (193.5±172.2 versus 16.1±13.1, P< 0.01).

Page 11; Paragraph 2; Sentence 4: "sulbenicillin became the first antibiotic canceled by DTC" Did you mean that the antibiotic was made unavailable or restricted?

Author response: we have polished according to reviewer’s suggestions. Sulbenicillin was made unavailable in outpatient service.

-----“193.5±172.2 CNY versus 16.1±13.1 CNY, P< 0.01”

-----“Finally, the DTC eliminated sulbenicillin from the antibiotic formulary for outpatient clinical practice”.

Referee 1 EVALUATION

Discretionary Revisions:

Page 9; Paragraph 3: The practice of fining practitioners is not common, and I find it interesting. Could you include more information on the numbers of inappropriate antibiotics the physician had prescribed?

Author response: Thanks very much for Joshua Courter’s professional suggestions. We have revised the relevant content completely according to the referee’s suggestions.

----- “During the study period, sixty-one physicians were fined due to inappropriate prescribing. One surgeon received a fine of 13000 CNY at a monthly DTC meeting following audit-feedback. The inappropriateness of antibiotics prescribed by this surgeon was reflected in improper combination antibiotic treatment (19 prescriptions), lack of clear clinical features of infection plus improper combination antibiotic treatment (26 prescriptions), off-label use (2 prescriptions), inappropriate antibiotic choice (1 prescription), and inappropriate antibiotic choice plus improper combination antibiotic treatment (3 prescriptions). For example, he prescribed isepamicin sulfate-levofloxacin combination for a patient with enlarged axillary lymph nodes in the right axillary region, ceftizoxime-levofloxacin combination for treatment of lower extremity infection, and cefotiam-isepamicin sulfate-ornidazole combination for patient with acute appendicitis.”

Other revision
1. Spelling check has been used again. English polishing has been conducted to our best.

2. The order of references was readjusted. Three references were added.


Dear Dr Catherine MT Sherwin, thank you very much for your professional arrangement of the two reviewers. These two reviewers are very professional, highly industrious, and extremely responsible. The reviewing work consumed them a lot of time and energy. Please remember me to Dr. Nithima Sumpradit and Dr. Joshua Courter. Their generosity and internationalism spirit really impressed us. Also, we thank Ms Ma. Celine Zapanta for her kind E-mail notice.

We fortunately submitted this paper to BMC Pharmacol Toxicol which undoubtedly has a very professional, generous, selfless team. We absolutely believe this journal will become an influential international journal with high impact factor.

We tried our best to revise the manuscript. We hope that our resubmitted paper has a significant improvement in quality after careful revision based on valuable suggestions from reviewers and editors. We would appreciate very much if our paper will be finally accepted.

If further revision is needed or you have any questions, please do not hesitate to contact me.

Thank you very much!

Sincerely yours

Quan Zhou, PhD, MHA, Professor, Clinical pharmacy specialist
Department of Pharmacy, the 2nd Affiliated Hospital, School of Medicine, Zhejiang University
Zhejiang 310009, China.
E-mail: zhouquan142602@zju.edu.cn