

Author's response to reviews

Title: Antimicrobial stewardship of Chinese Ministry of Health reduces multidrug-resistant organism isolates in critically ill patients: A pre-post study from a single center

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Version: 1 Date: 25 Aug 2016

Author's response to reviews:

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Aug 23, 2016

Giovanni Battista Orsi, Editor

BMC Infectious Diseases

Manuscript ID: INFD-D-16-00382

Dear Dr. Giovanni,

We wish to thank the two reviewers for their many helpful comments on our manuscript (Manuscript ID: INFD-D-16-00382, title: “Antimicrobial stewardship of Chinese Ministry of Health reduces multidrug-resistant organism isolates in critically ill patients: A pre-post study from a single center”).

Below, we have provided point-by-point responses to all of the reviewers’ comments. We have also enclosed a revised version of the manuscript.

We hope that our manuscript is now suitable for publication in BMC Infectious Diseases and we look forward to hearing from you.

Sincerely,

Haibo Qiu, M.D., Ph.D.,

Reviewer #1:

1. The manuscript described a technically sound piece of scientific research with data that supports the conclusions.

Author response:

We thank the reviewer so much.

2. There was information missing or confused from this paper that would allow the evaluation of the robustness of the results and findings.

The following are some data gaps:

Q1.MDRO decreased along with reduced consumption of antibiotics. If the category, doses, duration of antibiotic changed during the intervention?

Author response:

We thank and quite agree the reviewer`s recommendation. We checked and calculated the category, doses, duration of antibiotics. During the intervention, the category of antibiotics did not change (Table S1). The median duration of antibiotics were 3.64 (1.96, 6.18) and 3.42 (1.65, 6.19) before and after antimicrobial stewardship, respectively. The dose of antibiotics also did not change during the intervention. We added these results in our manuscript.

Table S1 The category of antibiotics before and after antimicrobial stewardship

Category	Before management	After management	p value
All, n	62	60	
Penicillins, n (%)	7 (11.29)	9 (15.00)	0.544
Cephalosporins, n (%)	18 (29.03)	18 (30.00)	0.907
Carbapenems, n (%)	3 (4.84)	3 (5.00)	0.967
Fluoroquinolones, n (%)	8 (12.90)	6 (10.00)	0.615
Aminoglycosides, n (%)	4 (6.45)	4 (6.67)	0.962
Macrolides, n (%)	4 (6.45)	4 (6.67)	0.962
Anti-fungi drugs, n (%)	7 (11.29)	7 (11.67)	0.948
Other, n (%)	11 (17.74)	9 (15.00)	0.683

Q2.Although the proportion of patients colonized or infected with MDRO decreased along with reduced consumption of antibiotics. But the author did not represent if the rate of Healthcare-associated infection of patients (including non-MDRO) was increased or decreased.

Author response:

We quite agreed the review`s suggestion. During the intervention, we also monitored the incidence of ventilator associated pneumonia (VAP), catheter related blood stream infection (CRBSI) and catheter associated urinary tract infection (CAUTI), which were the most common of health-care-associated infections (HCAIs) in our ICU. We found that the incidence of VAP was significantly decreased after the intervention. However, the incidence of CRBSI and CAUTI did not change after the antimicrobial stewardship (Table S2). We added these results in our manuscript.

Table S2 The incidence of HCAs before and after antimicrobial stewardship

HCAIs	Before management	After management	p value
VAP, n (‰)	24 (12.38)	19 (5.52)	0.007
CRBSI, n (‰)	14 (4.02)	19 (3.71)	0.819
CAUTI, n (‰)	8 (2.04)	11 (1.75)	0.742

HCAIs: health-care-associated infections. CAUTI: catheter associated urinary tract infection. CRBSI: catheter related blood stream infection. VAP: ventilator associated pneumonia. Incidence of VAP, CRBSI and CAUTI were defined as the number of VAP, CRBSI and CAUTI patients per 1000 ventilation days, per 1000 central venous catheter days and per 1000 urine-catheter days, respectively.

Q3.Line 116 and 117: During the study period, we practiced infection control measures according to the recommendations of the Centers for Disease Control (CDC). Is it U.S. or China?

Author response:

We were so sorry that we did not describe it clearly. We practiced infection control measures according to the recommendations of CDC of the USA. We marked the reference in our manuscript.

Q4.Line 133: MDRO were defined as bacteria were resistant to at least three antimicrobial classes. Please mark the reference of MDRO definition.

Author response:

We thank and quite agree the reviewer`s recommendation. The MDRO definition was according to the definition which created by European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC) of the USA (Clin Microbiol Infect 2012; 18: 268–281). We marked the reference in our manuscript.

Q5.In Table3,the figures in parentheses represent quantity, rate or proportion, which one? If it is proportion, please correct to two decimal places.

In Table3,all patients is 220,but before and after management is 154 and 71,please correct it.

Author response:

We were so sorry that we made this mistake. In table 3, the figures in parentheses were proportion. We corrected them to two decimal places. We also corrected the number of all patients 220 to 225 (please see the detail in Table 3 in the manuscript).

Reviewer #2:

- 1) Background. Suggest on removing the first paragraph of the background and starting with second paragraph.

Author response:

We thank and quite agree the reviewer`s recommendation. We removed the first paragraph.

- 2) Background. Line 70. Further expand on what policies were implemented by China to improve antimicrobial usage.

Author response:

We quite agree the reviewer`s the suggestion. Because the detail of policies in China to improve antimicrobial usage was describe in the Methods, we introduce these policies briefly. We added the sentences ‘These policies included restricting the kinds of antibiotics, setting the targets for antibiotic prescription in hospitalized patient and prophylactic use of antibiotics in clean operations (Please see the detail of polices in methods of Antimicrobial stewardship)’ in the manuscript.

- 3) Methods. Was there any rapid diagnostics tests? If so, which ones?

Author response:

We did not use any rapid diagnostics tests.

- 4) Methods. Describe whom are all part of the antimicrobial stewardship team...pharmacist ID trained? ID physician? Microbiologist? Infection preventionist?

Author response:

We thank the reviewer to point this question. The trained pharmacist and infection preventionist were all part of the antimicrobial stewardship in our hospital. We revised it in the manuscript.