Reviewer’s report

Title: Intravenous to oral antibiotic switch therapy: a cross-sectional study in critical care units

Version: 1 Date: 09 Apr 2019

Reviewer: Giorgia Montrucchio

Reviewer's report:

Dear Authors,

I review the new version of your manuscript INFD-D-18-02192R1.

As previously mentioned, the topic is of particular interest and the possibility of shift to oral therapy is a strategy hardly applied to critically ill patients.

You have modified many aspects of the manuscript according to the suggestions proposed, and it is certainly improved compared to the first version.

However, in my opinion, some substantial clarifications are indispensable.

- You defined the study a cross-sectional study. As suggested by the reviewer 1, I would say it is a retrospective cohort study (the analysis was retrospective with a convenience sample).

- The discussion still seems rather inadequate and not well organized. Some logical passages are missing, and perhaps due to linguistic problems it does not clearly show the possible reasons for the results obtained.
I request the following clarifications with respect to yours replies:

- "The AS program included not only oral switch, but also a complete program, including de-escalation, dose adjustment, and others. However, the analysis included only the comparison of patients with oral switch and those whose intravenous therapy was maintained. Patients with other interventions were excluded."

In this case, I think it is important to explain in the methods that the shift is a part of a more inclusive strategy and to clearly describe the possible impact of other interventions on the evaluated switch (if not investigated, add in the limits).

- "This is an important limitation because the groups are not similar. We included this limitation in the discussion. The only way to perform similar groups would be an RCT, which is our objective after this study, because we need the background of this study for RCT. I believe that a real randomization is not possible in this case, also for ethical reasons as well as statistics. I think it is more correct to say that the sample of patients subjected to oral shift has in itself different characteristics, generally of lower clinical severity and of less bacteriological complexity and resistance. Therefore, only the possible pejorative impact on mortality is investigated."

- "In the table 2, the line "IV Antibiotic duration (days)"

About the extent to which the shift takes place - after how many days of treatment, with which microbiological correlation- I think will be important to discuss this data more extensively, because the duration of the previous treatment can define the complexity of the infection.

- "We included the formulation of each oral drug. The choice of oral therapy was defined during the rounds according with with cultures, site, organ dysfunction and possible side effects."

Please, specify in the methods.
- "We did not discussed (? discuss) about impact on resistance"

Also in the abstract it is emphasized that the group subjected to oral shift has less resistance, but the connection is contrary to what was stated. It is useful to clarify that the lower resistances allow shift, not that the shift causes less resistance.

Please pay attention to the following notes:

Abstract:
1. Page 2, line 50: incomplete sentence
2. Page 2, line 51: "these patients": not clear
3. Page 2, line 52: "following an inclusion criteria" not clear, please specify
4. Page 2, line 54: "daily costs" not mentioned in the results; here you did not mention AKI, that you discuss in the results.
5. Page 2, line 55: "no intervention": better use no oral shift
6. Page 2, line 59: incomplete sentence, not understandable

Background:
The paragraphs are poorly connected, not logically connected. Maybe I suggest to change the order (I propose to postpone AS - page 3. Line 73- after line 86).
1. Page 4, line 96: I would stress the importance of safety and the assessment of mortality

Methods:
1. Page 5, line 104: I believe it is essential to mention the retrospective nature of the study
Discussion:

1. Page 14, line 283: stewardship program: I suggest "stewardship intervention"

2. Page 14, line 285: the groups: please specify

3. Page 14, line 288: although the total cost of hospitalization did not show any difference: please, try to explain

4. Page 14, line 288 and following: "Taking (…) inadequate": this sentence seems not logically connected to the previous ones.

5. Page 14, line 294: 20% is referred to your ICU or to literature? Not clear.

6. Page 15, line 306: I suggest that the incidence of AKI deserve a more complete discussion.

7. Page 15-16: logically repeated and disorganized concepts. I suggest reordering the topics and avoiding repetitions.

8. Page 16, line 354: as previously said, I don't know if a real randomization will be ethically possible…


10. Page 17, line 360 and following: I consider this one the first and most important limit, please, try to better explain this concept (without randomization).
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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