

Dear Editors:

Thank you for your letter and for the comments concerning our manuscript entitled “Early Administration of Arbidol Found Beneficial with Covid-19 Patients:A Retrospective Cohort Study” (ID:65342). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important in guiding our researches. We have studied comments carefully and have made corrections. And we have also made corresponding adjustments according to the format of the journal.

The main corrections in the paper and the responses to the reviewer’s comments are as follows:

Reviewer 1:

First of all I would like to compliment the authors, as the study provides important information about the potential therapeutic use for arbidol in mild-to-severe COVID-19 patients, and studies the correlation between the early use and its beneficial effect. Review: Minor review of the grammar is needed (connectors, punctuation and spacing between words). There are sentences that are redundant, hard to read or doesn’t fit the context of the text. • The word “covid-19” goes in Capital letters: COVID-19 • RT-PCR section should be included in the case definition section and describe that the RT-PCR is for SARS-CoV-2. • Case definition, RT-PCR, treatment plan, discharge criteria, Participants, data collection sections, should be in methods section. • Line 79: “The prognosis is good” is redundant. • Line 80: “Approximately 1/5 to 1/10 patients will require in-patient admission, and the predictors are age and underlying disease.” This sentence is hard to read, suggestion: “Approximately 1/5 to 1/10 of the patient with old age or an underlying condition will require in-patient admission” • Line 119: “Jinyintan Hospital and Huoshenshan Hospital is an infectious disease hospital in Wuhan, China.A total of 132 patients of 18 years old and over who met the Covid-19 diagnostic criteria and treatment program were included from moderate to severe patients. Excluding mild clinical forms and critically ill patients.” This paragraph is hard to read, suggestion: “Patients from the Jinyintan Hospital and Huoshenshan Hospital, which are infectious disease hospital in Wuhan, China, were recruited for the study. A total of 132 patients above 18 years old, who met the diagnostic criteria for moderate to severe presentation of COVID-19, and Arbidol treatment program were included. While Mild clinical forms and critically ill patients were excluded” • Line 145: “The treatment plan is determined by the doctor on duty, with or without Arbidol , the directions for use are 200mg for adults, 3 times a day with a 10 days course of treatment and not receiving any other drugs.” this paragraph is hard to read, suggestion: “The treatment plan is determined by the doctor on duty, the directions for Arbidol use are 200mg for adults, 3 times a day with a 10 days course of treatment and not receiving any other drugs. • Line 148-152: “We looked for the early stages of sudden outbreak of the epidemic, places of limited medical resources, limited ward beds and delayed admission, so there are some patients cases naturally fit in the control group which did not receive any antiviral drugs. Compare the disease course of the two groups; and explore the predictors for long disease duration.” This paragraph is hard to understand, separate and explain the variables. • Line 162: “Statistical analyses were done using the IBM SPSS Statistics (version 23.0).Compare the baseline data of the two groups” suggestion: “Statistical analysis was done using the IBM SPSS Statistics (version 23.0) to compare the baseline data of the two groups” • Line 164: “compare the various factors of the long and short disease duration” suggestion: “we compared the various factors of the long and short

disease duration. • Line 171: “. Use single and multi-factor analysis to analyze the independent risk factors that affect the course and duration of disease” this sentence is redundant, suggestion: we used single and multi-factor analysis to study the independent risk factors that affect the course and duration of disease. • Line 177: “Effects of using Arbidol, Divided into intervention group: 72 patients who used Arbidol; control group group: 60 patients who did not receive any antiviral drugs”. suggestion: In order to analyze the effects of using arbidol, we formed 2 groups of study: intervention group: 72 patients who used Arbidol and control group: 60 patients who did not receive any antiviral drugs. There are multiple studies regarding the still controversial effect of arbidol (umifenovir), a comparison between the findings in the study and the results of contraposition articles, can further improve the quality of the discussion section in the manuscript. Suggested bibliography: • Evaluation of current medical approaches for COVID-19: a systematic review and meta-analysis; Meng Wang, Ting Wu, Zhihong Zuo, Yaxian You, Xinyuan Yang, Liangyu Pan, Ying Hu, Xuan Luo, Liping Jiang, Zanxian Xia, and Meichun Deng. DOI: <http://dx.doi.org/10.1136/bmjspcare-2020-002554> • Efficacy and safety of umifenovir for coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis; Dong Huang He Yu Ting Wang Huan Yang Rong Yao Zongan Liang DOI: <https://doi.org/10.1002/jmv.26256> • Clinical efficacy of antivirals against novel coronavirus (COVID-19): A review; ShahamahJomahSyed Mohammed Basheeruddin, Asdaq Mohammed, JaberAl-Yamani DOI: <https://doi.org/10.1016/j.jjiph.2020.07.013> • Umifenovir treatment is not associated with improved outcomes in patients with coronavirus disease 2019: a retrospective study; N.Lian, H.Xie, S.Lin, J.Huang, J.Zhao, Q.Lin. DOI:<https://doi.org/10.1016/j.cmi.2020.04.026>

Response:

Thank you very much for your approval of our work. We have modified all the sentences according to the reviewer's suggestion. In view of the bibliography suggested by the reviewer, we have made a careful analysis, and cited the results of some references in the discussion section (reference No.13) .

Reviewer 2:

Authors showed reduction on the time of recovery of patients with moderate to severe COVID-19 when treated with Arbidol. In the Aims of the abstract I suggest to specify the disease. "... Arbidol against COVID-19" Methods in the abstract mentioned just one Hospital but in the main text two hospitals are mentioned. In the discussion of the main text, approximately in the ninth line, spinosin is mentioned. I think, authors want to mention Spike protein instead. I recommend in table 2, add the distribution of moderate cases. I know that is possible to infer it just taking into account the Severe cases but I think is better to explicitly show moderate cases distribution.

Response:

Thank you very much for your suggestions. We specify “COVID-19” in the Aims of the abstract. “Methods in the abstract mentioned just one Hospital but in the main text two hospitals are mentioned”, In the methods section of the abstract, we have added another hospital (Huoshenshan hospital), “In the discussion of the main text, approximately in the ninth line, spinosin is mentioned, I think, authors want to mention Spike protein instead”, we have changed spinosin to spike glycoprotein. “ I recommend in table 2, add the distribution of moderate cases”, we have

added distribution of moderate cases in talbe 2.

The quality of the language of our articles have been polished by the “**AJE**” company,we tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

We would like to express our great appreciation to you and reviewers for comments on our paper. Looking forward to hearing from you.

Thank you and best regards.

Yours sincerely,

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