Clinical Infectious Diseases

CORRESPONDENCE

Answer to Letter Concerning the Paper "Double-Blind, Randomized, Placebo-Controlled Trial with N-acetylcysteine for Treatment of Severe Acute Respiratory Syndrome Caused by COVID-19"

To the Editor—First, we would like to thank Professor Lapenna for the comments about our article.

We agree with most of his remarks, and we had already approached some of them when we discussed the limitations of our study [1].

Regarding N-acetylcysteine (NAC) administration's timing, we believe that antioxidants could work if given before the lung disease was established.

However, this preventive treatment would not be feasible. Considering that most patients with Covid-19 do not develop pneumonia [2], it would be necessary to administer NAC in high doses to a large number of asymptomatic or oligosymptomatic individuals. It would be costly and ethically debatable. Therefore, we opted to treat only patients with mild hypoxemia, and, in these cases, NAC did not work, unfortunately.

The second comment is related to the use of a standard NAC preparation. We agree with Professor Lapenna that a hydrophilic NAC preparation was not ideal for acting as an intracellular antioxidant. It was selected based on our previous experience with the drug and its availability. The liposomal NAC seems to be an interesting approach, but we did not have the technology readily available and did not have the time to develop it in our institution. Besides that, NAC has been used for treating acute liver failure and proved to be highly effective and accessible to the intracellular environment [3].

Adding another antioxidant (for example, vitamin E) could be an alternative, but we believe it would also bring more risks and collateral effects. A recent meta-analysis pointed out that high-dosage (≥400 IU/d) vitamin E supplements may increase all-cause mortality [4].

In conclusion, we agree that our study has some limitations; however, considering the urgency and safety required, it brought important information about Covid-19 treatment. Future clinical trials involving antioxidant drugs to treat Covid-19 should take into consideration our failure and build upon our results.

Note

Potential conflicts of interest. Neither author has any potential conflicts to disclose. Both authors: No reported conflicts of interest. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases® 2021

DOI: 10.1093/cid/ciab056