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Correspondence

Letter to the Editor: Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019 in Korea: the Application of Lopinavir/Ritonavir for the Treatment of COVID-19 Pneumonia Monitored by Quantitative RT-PCR

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▸ See the article "Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019 in Korea: the Application of Lopinavir/Ritonavir for the Treatment of COVID-19 Pneumonia Monitored by Quantitative RT-PCR" in volume 35, number 6, e79.

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I am grateful that Dr. Lim and his colleagues reported a case of COVID-19 that caused tertiary transmission in Korea and added information about the novel infectious disease.[1] In this report, the authors emphasized the decrease in viral titer due to the effects of antiviral administration. However, I would like to discuss what to look out for when interpreting the causal relationship between laboratory results and therapeutic effects.

Lopinavir and ritonavir (LPV/r) is considered a promising treatment option for COVID-19 based on the 2003 SARS treatment experience.[2,3] However, care should be taken when administering because there are no or little clinical evidence for the new virus, SARS-CoV-2. I have treated with LPV/r as an antiviral agent in patients with pneumonia caused by COVID-19, but the disease course has not improved dramatically.[4] Fortunately, the patient did not develop acute respiratory failure, but it was not clear whether it was an effect of antiviral drug.

According to the Center for Laboratory Control of Infectious Diseases in KCDC, the upper limit of Ct value for positive RT-PCR of SARS-CoV-2 is 35, and the negative criterion is Ct value 37 or higher. In this case report, it is difficult to determine that the test result is positive because the Ct value is 35.66 on day 10, the day of the antiviral treatment. If there was a virus, it would have remained a very low titer. Since LPV/r was administered during the virus titer reduction from 30.71 (day 9) to 35.66 (day 10), I think two consecutive negative results are more likely to be due to the natural history of the disease than to antiviral agents. Furthermore, the authors did not explain why Ct values are consistently detected near positive criteria from day 4 of treatment despite the continued use of antiviral agents.

The authors say they do not know whether the decrease in virus titer is a natural course or antiviral effect, or both. However, the authors are making a leap of logic that LPV/r

administration reduces viral load. Also, the authors explain that LPV/r administration has also improved clinical symptoms. However, The fever has already been falling from the day before, and the cough lasted for few more days. Since LPV/r was given to patients on day 10, it could not be regarded as being administered in the early stages of the disease. However, the authors argue that antivirals should be given early in the disease, based on this case. For the reasons described so far, it is difficult to say that LPV/r lowers the virus level or improves symptoms or is "recommended" for COVID-19 treatment based on this case report alone.

Regardless of the case report, I still believe that LPV/r is a promising antiviral agent for the treatment of COVID-19. However, it is clear that well-designed studies have to be carried out to build more evidence so that they can be recommended as therapeutic agents.

Research is a very important component of the response during an outbreak. But even if the epidemic is underway, we should reiterate that we should try to find evidence based on a scientific background, and be careful to advise what is not.

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Response

The Author's Response: Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019 in Korea: the Application of Lopinavir/Ritonavir for the Treatment of COVID-19 Pneumonia Monitored by Quantitative RT-PCR

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I appreciate Dr. Kim's interest in our article entitled "Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019 in Korea" and we would like to thank him for his critical comment to improve our article.[1]

Our report focused on the decrease of virus loads and the alleviation of the patient's symptoms during lopinavir/ritonavir (LPV/r) administration. As Dr. Kim mentioned in the letter, our findings did not prove whether it was caused by the natural course of the disease or by the effects of drug and there is no clinical evidence. We did not argue that the decline of viral load was caused solely by the antiviral agent we used and emphasize that broader clinical trials will be needed to reveal the therapeutic efficacy of this study of this antiviral agent.

Unfortunately, no drug or vaccine has yet been approved to treat coronavirus disease 2019 (COVID-19). Favipiravir, ribavirin, remdesivir and galidesivir could be good candidates as potential antiviral agents for the treatment.[2] And many clinical trials on anti-HIV drugs, LPV/r and experimental antiviral agent, remdesevir are in the development process in China (http://clinicaltrials.gov/show/NCT04261907, http://clinicaltrials.gov/show/NCT04255017).[2] There are reports that remdesevir and antimalarial agent, chloroquine effectively inhibited SARS-CoV-2 in vitro.[3] If these clinical studies are successful, they can provide us with more efficient treatment options and suggest better choices for COVID-19 treatment in high-risk groups (elderly patients or patients with underlying diseases).

Disclosure

The authors have no potential conflicts of interest to disclose.

What we discussed in this report is the relative quantitation of virus loads with qRT-PCR during LPV/r administration and alleviation of the patient's symptoms. Therefore, if better and broader clinical trials monitored by qRT-PCRs are designed and performed during antiviral agent administration, more accurate viral kinetics of COVID-19 will be obtained and the effects of the drug will be elucidated more clearly.

We are hoping that the outbreak may subside in a couple of months, with the consistent efforts to prevent the spread of COVID-19 worldwide, as in the cases of SARS and MERS. In the meantime we need to make great efforts to develop antiviral agents to treat COVID-19 as well.

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