

Letter to the Editor

Comment on safety and efficacy of oral lopinavir/ritonavir in pediatric patients with coronavirus disease: a nationwide comparative analysis

Dear Editor,

during 2020 the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemics halted the entire World¹. On the other hand, research had an incredible surge of enthusiasm and frenzy, leading to different possible solutions to the pandemics².

Clinicians and researchers first tried to repurpose old drugs for a new danger. This was the case with lopinavir/ritonavir (LPV/r), a combination of antiretroviral drugs inhibiting HIV protease enzyme³⁻⁵. A number of studies, both *in vitro* and *in vivo* ones, showed that LPV/r might have an effect on SARS-CoV-2⁶. Therefore, LPV/r was introduced for the treatment of coronavirus infectious disease 2019 (COVID-19)⁶.

LPV/r was also used in a pediatric subpopulation of COVID-19 patients, despite it being quickly contraindicated in this subpopulation⁷. We read with great interest the paper of Lu et al⁸ concerning safety and efficacy of LPV/r in pediatric patients. They included in their study 23 COVID-19 pediatric patients, treated for at least 5 days with oral LPV/r according to their weight. Matching 92 controls that were treated with standard of care, such as cough syrup and interferon atomization treatment, they showed that not only LPV/r fails in improving the children's health conditions, but it also slows down viral clearance and the discharge process.

Similarly, Pan et al⁹ reported that the use of LPV/r was associated with prolonged viral shedding in a population of adults in univariate analysis. However, the multivariate analysis showed a possible protective role against prolonged viral shedding of LPV/r. A case series presented by Luo et al¹⁰ supports the protective role of LPV/r against prolonged viral shedding.

LPV/r has been recommended as a therapeutic choice for COVID-19 patients during most of the "first wave", although being rapidly dismissed due to side effects and drug-to-drug interactions. Moreover, contrasting evidence raised from *ad interim* and retrospective studies, since LPV/r was used in different associations with other reportedly useful agents. Many confounding factors made it impossible to determine if the LPV/r was actually effective in treating COVID-19, especially in children.

In conclusion, LPV/r possibly represented a good choice to treat SARS-CoV-2. However, its misuse and drug cocktails made it not possible to understand to which extent. Moreover, high-prevalence of adverse events in children, combined with the results of Lu et al⁸, confirm that the drug should not be used in pediatric cases.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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