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Comments on the Pathophysiological Basis and Rationale for Early Treatment of COVID-19



To the Editor:

We have read the review article by McCullough et al¹ about early outpatient treatment of coronavirus disease 2019 (COVID-19) and would like to make some comments and raise some questions.

Several highly respectable entities worldwide do not recommend early outpatient treatment because of the lack of proven benefits and the potential for adverse effects.²⁻⁶

We emphasize that we all will be in favor of early outpatient treatment for COVID-19 as soon as any drug demonstrates safety and effectiveness based on a randomized controlled trial. Studies based only on pathophysiology are not adequate to prove the benefit of drug intervention.

The article cited a retrospective study⁷ that was used as an evidence that favors the use of early treatment. It is worthwhile to highlight that the study showed the opposite: “treatment with HCQ, azithromycin, or both, compared with neither treatment, was *not* significantly associated with differences in in-hospital mortality.”

Dexamethasone was associated with reduction in mortality in patients with COVID-19 who require supplemental oxygen or ventilatory support. In early treatment, its use can be harmful.^{3,4,8-10} In addition, the dose used in RECOVERY Trial was 6 mg a day for 10 days.⁸ Thinking of equivalent doses of other glucocorticoids, we would have a total daily dose of prednisone of 37.5 mg. What are the scientific support data the authors used to recommend a higher prednisone daily dose of 1 mg/kg?

Correct azithromycin dosing, approved for bacterial respiratory infections, is 500 mg once a day as a loading dose, followed by 250 mg or 500 mg every day (throughout the whole treatment). What are the clinical and pharmacological data to recommend 250 mg twice a day?

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In conclusion, the desire to preserve lives in such a devastating public health crisis as the COVID-19 pandemic is understandable; however, it is essential to follow the best scientific evidence and the principles of bioethics.

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