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Unproven Therapy Algorithms for Early SARS-CoV-2 Infection Are Dangerous

To the Editor:

We read with interest the article by McCullough et al[1] about the pathophysiological basis and rationale for early outpatient treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which results in coronavirus disease 2019 (COVID-19). Although the article discusses some significant issues, it has many important drawbacks.

As the authors pointed out, there are "2 major areas of response to the pandemic: containment of the spread of infection and reducing inpatient mortality." The first relates to social distancing, mask use, hand hygiene, testing, and isolating infected people and their contacts. The second relates to treating patients who are hospitalized with support measures and drugs that have demonstrated some benefits, such as corticosteroids, and to managing critically ill patients with emphasis on mechanical ventilation. Outside these interventions, all drugs mentioned in the review should not be indicated as early outpatient treatment. Articles postulating such things have the potential to worsen outcomes because they give the false impression that there is an early treatment capable of saving the lives of people infected with COVID-19, and people may relax preventative measures. Brazil is an example of this horrible situation.

We understand that in a pandemic efforts should be directed to repurposing and developing drugs that might improve hard endpoints when introduced early. But in contrast to what the authors say, good evidence can be produced during a pandemic, and many studies have already shown that hydroxychloroquine,[2] azithromycin,[3] and favipiravir[4] have no beneficial effects on clinical outcomes in patients with COVID-19. The beneficial effects of corticosteroids were observed in patients receiving supplemental oxygen,[5] and not in those with respiratory symptoms alone or after the fifth day of illness as postulated in the treatment algorithm. There is also no indication to initiate anticoagulation based on suspected microthrombosis. Finally, a recent article on potential early treatments did not even mention hydroxychloroquine, azithromycin, or zinc.[6]

Algorithms have been used for decades as a clinical and teaching tool to improve patient care, but we fear that the impact of this article might have the opposite effect of its fundamental objective.

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