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Early Outpatient Treatment of SARS-CoV-2 (COVID-19): A Comment



To the Editor:

McCullough et al propose a treatment algorithm for early outpatient treatment of coronavirus disease 2019 (COVID-19), which is not supported by evidence.¹ Early intervention is desperately needed, but unfortunately, no effective treatment is available.²

Neither zinc (Zn) nor doxycycline have demonstrated inhibition of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in vitro or in animal or human studies. Favipiravir has antiviral activity against SARS-CoV-2 but does not have “proven” therapeutic efficacy in Ebola, Lassa fever, or rabies as claimed. Favipiravir should only be administered as part of clinical trials assessing efficacy and safety.

The Randomized Evaluation of COVID-19 therapy (RECOVERY) trial proved that large clinical trials can be completed rapidly during a pandemic. Dexamethasone was associated with reduced mortality for patients receiving invasive mechanical ventilation or supplemental oxygen but not for patients receiving no respiratory support at randomization.³ Possible efficacy of prednisone in early disease is unproven speculation that cannot be recommended without further study.

McCullough et al recommended “antivirals” hydroxychloroquine (HCQ) and azithromycin (AZ) “immediately” for high-risk patients, but HCQ did not show antiviral activity in human airway epithelium, and neither HCQ nor HCQ with AZ showed a significant effect on SARS-CoV-2 viral load in macaques.⁴ In a meta-analysis (total participants n = 32,943), HCQ was not associated with reduced mortality in hospitalized patients, but HCQ with AZ significantly increased mortality.⁵ Observational studies in which HCQ

with or without AZ was associated with reduced mortality include important confounders (concomitant corticosteroid use in the HCQ group, more than double the nontreated group).⁶ Early treatment of outpatients with mild disease with HCQ with or without AZ has not demonstrated clinical or virological benefit, and no significant reduction of risk of hospitalization.⁷

Facing mounting contrary evidence, the proponents of HCQ with AZ resemble the deluded Black Knight from *Monty Python and the Holy Grail* whose limbs are progressively cut off but continues to confidently proclaim triumph in the battle.

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