



Colchicine as a possible therapeutic option in COVID-19 infection

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Dear Editor,

We reviewed the manuscript recently published by Cumhur Cure M, et al. [1], regarding colchicine and COVID-19. The authors discussed the effects of colchicine in intracellular and extracellular pH conditions and argued that low pH levels secondary to colchicine may increase the viral load of SARS-CoV-2 and, therefore, cytokine storms will be more severe.

In contrast, we consider that colchicine can be a good therapeutic option because of several effects in the immunology system involved in SARS-CoV-2 infection and in the acute respiratory distress syndrome (ARDS). Colchicine has effects on the chemotaxis of inflammatory cells such as neutrophils and monocytes and on the intracellular transportation of vesicles such as endosomes and exosomes. Colchicine also inhibits the expression of E-selectin, an adhesion molecule important for binding leukocytes to endothelial cells, and the recruitment of monocytes and neutrophils to inflamed tissue. Finally, colchicine reduces neutrophil production of free radicals like superoxide [2]. The recruitment of neutrophils in COVID-19 is a key factor in the severity of cases [3]. Moreover, colchicine has also been associated with disrupting

inflammasome activation, thereby suppressing caspase-1 activation and the subsequent release of IL-1 β and IL-18 [4]. In SARS-CoV-1, the inflammasome activation has been associated with this disruption [5].

The authors also cited an article published in 1986 by Maurizi M, et al. [6] regarding two patients who developed ARDS after treatment with toxic doses of colchicine. The first patient received approximately 80 mg of colchicine or 1.6 mg/kg, while the other patient received 15 to 20 mg or 0.25–0.3 mg/kg of colchicine for acute gout. Both patients had ARDS between 24 and 72 h after the colchicine doses [1]. Both articles [1, 6] attributed a direct toxic action of colchicine on pneumocyte microtubules, and the inhibition of surfactant production was deemed the probable cause of death of those patients. The dose used in those cases is not recommended due to the toxicity. The usual adult oral dose in acute gout is 1.2 mg/day or as a prophylactic, 0.5–1 mg/day; however, dose must be adjusted in patients with renal impairment. The high fatality rate was reported after acute ingestions exceeding 0.5 mg/kg [7], and therefore, there is no support for that outcome in therapeutic doses.

Classically colchicine is commonly used to treat different inflammatory diseases such as gout, as well as some autoinflammatory diseases, and cardiac conditions including viral pericardial syndromes. Recently, a patient with cardiac tamponade secondary to COVID-19 was treated with colchicine in addition to corticosteroids and antimalarials with positive clinical response [9]. Other research demonstrates the positive effect of colchicine in respiratory syncytial virus replication and suppression of secondary airway inflammation given the promoted expression of IFN- α and IFN- β 1 of colchicine and regulation of anti-oxidative factor production [10, 11]. In addition, there is a wide range of preclinical and clinical literature on the effect of colchicine inhibiting viral disease like adenoviral and adeno-associated viral [12], herpes simplex virus type 1 [13], Epstein-Barr virus [14], and hepatitis virus [15, 16], among others.

On the other hand, Cumhur Cure M, et al. [1] discussed the interactions of colchicine with other drugs. We would agree

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that colchicine may indeed have interactions with other drugs; therefore, we recommend adjusting the dose in close consideration of the interactions with inhibitors of CYP3A4 as antibiotics and antivirals even though some of them are used in COVID-19 as lopinavir/ritonavir.

In our experience, we reported 5 patients (age 38–61 years) with comorbidities (arterial hypertension, type 2 diabetes, among others) in treatment with colchicine for iatrogenic allogeneic 1 to 3 weeks before COVID-19 test positive. They developed mild symptoms such as headache, cough without dyspnea, and arthralgias. It should be noted that some close contacts presented severe symptoms and three of them died [8].

According to a potential benefit of colchicine in COVID-19 patients, since March 26, 2020, a total of twelve studies have been registered in www.clinicaltrials.gov and the European Union Clinical Trials Register considering the clinical utility of this well-known medication. Most of these studies correspond to randomized, open-label, phase 2 clinical trials. It is aspired to include more than 11,000 patients on three continents. The experimental arm in most studies includes an oral colchicine regimen with loading and maintenance doses plus the standard of care for COVID-19. Primary outcomes to evaluate include change in clinical condition (according to the semiquantitative ordinal scale suggested by WHO), requirement for invasive mechanical ventilation/intensive care unit, delta in the score for the Sequential Organ Failure Assessment, length of hospital stay, all-cause mortality, and change in prognostic biomarkers. The evaluation of these outcomes will be carried out in a time frame up to 30 days, and hopefully, their results will be available soon.

Compliance with ethical standards

Disclosures None.

Informed consent Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

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