LETTER TO THE EDITOR

Comment on "Colchicine may not be effective in COVID-19 infection; it may even be harmful?"

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Dear Editor

We read with great interest the report by Cure et al. which speculated that colchicine may not be effective in COVID-19 infection [1]. The main argument of the authors is that colchicine may have not increased the intracellular pH enough and cannot prevent the binding of the virus to the target angiotensin converting enzyme 2(ACE2) receptors. Also, they suggest that colchicine may increase the risk of acute respiratory distress syndrome(ARDS) and disseminated intravascular coagulation(DIC) which may occur during COVID-19 infection. We have not agreed with the authors at these points. First, the colchicine and anti-malarial drugs both may increase the intracellular pH by different mechanisms. There are no studies investigating the intracellular concentration of colchicine in corona infection, while such data exist regarding chloroquine [2]. So, this view is only an author's hypothesis that is not based on scientific data. Second, there is no any data supporting Cure et al. that colchicine increases the risk of ARDS and DIC in COVID-19 patients. On the contrary, we hypothesize that colchicine may protect rheumatic patients from COVID-19 or perhaps cause them to pass in a milder form of disease. COVID-19 is not only a viral infection, it is an autoinflammatory/autoimmune process that develops as a result of immune system dysfunction, cytokine release syndrome, and hemophagocytic lymphohistiocytosis [3]. It acts by binding to ACE2 receptors in target organs such as lung alveolar type 2 cells [4]. When COVID-19 is passed into the cell via ACE2, activation of NLRP3 inflammasome is triggered by immunological mechanisms. The presence of high NLRP3-induced pro-inflammatory cytokines (IL-1, IL-1beta) in the sera of COVID-19 patients supports this hypothesis [5]. Colchicine is an anti-inflammatory agent that inhibit the microtubule polymerization on the cytoskeleton. Microtubules play an important role in cell migration, signal transduction and gene expression [6]. Colchicine act on NLRP3 inflammasome resulting in inhibition of important signaling pathways involving intracellular secretion of cytokines and chemokines. It is estimated that one of the important pathogenic mechanisms of COVID-19 is through activation of NLRP3 inflammasome [7]. Considering the mechanism of action of colchicine, it would make rationale use in patients with COVID-19 infection [8]. Therefore, at the present time, four randomized studies regarding colchicine in COVID-19 patients have been ongoing. ClinicalTrials.gov Identifier: NCT04322682, NCT04326790, NCT04322565, NCT04328480).

Recently, we reported COVID-19 infection in a patient with FMF under treatment with colchicine [9]. The patient was PCR positive for COVID-19 and have only mild symptoms of disease (such as myalgia, arthralgia). On radiologic investigation, thorax CT was normal. The patient was treated according to accepted protocol,(hydroxychloroquine, azitromycine, and oseltamivir) in our country. Colchicine was also continued. Markedly regression in patients complaints after treatment were seen and control COVID-19 PCR test was negative. Although we cannot draw any definitive conclusion from our observation, we hypothesize that colchicine may prevent of severe form of disease. Prospective, randomized, placebo-controlled studies are needed in this regard.

Compliance with ethical standards

Conflict of interest The author declared not any conflict of interest of any financial support.

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