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Mini Review

Role of Colchicine in Management of COVID-19?

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Abstract: CoV-2 disease 2019 (COVID-19) pandemic has exerted a great burden on the health and economic systems worldwide. One of the most important factors that affect the severity and prognosis of COVID-19 is the occurrence of hyperstimulation of the immune system resulting in "cytokine storm". Similar to SARS-CoV, an intracellular complex called nod like receptor family pyrin domain containing 3 (NLRP3) inflammasome was found to be activated by SARS-CoV-2, then in turn stimulates several interleukins and initiates the inflammatory cascade. In addition, other inflammatory mediators such as interferons e.g., IFN-α, and IFN-γ, interleukins e.g., IL-1β, IL-12, IL-18, tumor necrosis factor-α (TNF- α), and chemokines e.g., CCL2, CXCL10 have been reported in severely ill patients. These mediators represent the corner stone in developing cytokine storm that results in uncontrolled systemic inflammatory reaction with subsequent acute respiratory distress syndrome (ARDS), multiple organ failure and eventually death. Based on its anti-inflammatory effects, colchicine has also gained attention to be utilized in the management of COVID-19 patient. Colchicine exerts its anti-inflammatory effect through inhibition of formation of microtubules which is considered an essential step in several cellular processes such as division, signalling, and migration. Also, colchicine affects the cytokine cascade by inhibiting IL-1β leading to reduction in neutrophils recruitment, free radicles production and inflammasome stimulation. This raises the concerns about the effectiveness of colchicine in COVID-19 treatment and the possibility of providing an improvement of the clinical course of the disease.

Keywords: Coronavirus, COVID-19, Colchicine, Management, Review

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CoV-2 disease 2019 (COVID-19) pandemic has exerted a great burden on the health and economic systems worldwide. COVID-19 is caused by SARS-CoV-2 which belongs to coronaviruses family that also includes SARS-CoV and MERS-CoV [1].

In China, SARS-CoV caused outbreaks of severe respiratory distress syndrome in 2002 and 2003 [2]. While in 2012, outbreaks of severe respiratory distress syndrome have been reported in the Middle East and was caused by MERS-CoV [3]. All coronaviruses including SARS-CoV-2 are characterized by the presence of S proteins in the viral envelope that surrounds the nucleocapsid formed of RNA and phosphorylated nucleocapsid protein [4]. S proteins are responsible for direct binding between the viral particles and host cell membrane through interaction with angiotensin converting enzyme 2 (ACE2) receptor, which is found in different tissues such as lung, kidney, heart, and intestine [5]. This can contribute to affection of COVID-19 to multiple body systems and clinical

presentation ranges from mild symptoms to severe cases of pneumonia, acute organ failure such as kidney, and ischemic events [6]. One of the most important factors that affect the severity and prognosis of COVID-19 is the occurrence of hyperstimulation of the immune system resulting in "cytokine storm" [7]. Similar to SARS-CoV, an intracellular complex called nod like receptor family pyrin domain containing 3 (NLRP3) inflammasome was found to be activated by SARS-CoV-2, then in turn stimulates several interleukins and initiates the inflammatory cascade [8]. Also, interleukin-6 (IL-6) has a role in inducing cytokine storm. IL-6 is produced by different immune cells under stimulation by tumor necrosis factor-α (TNF-α) and IL-1β. High levels of interleukin-6 result in activation of T helper 17 that triggers severe inflammatory response in COVID-19 patients. Furthermore, the level of IL-6 has been related to the severity of COVID-19 infection and used as a predictor of clinical prognosis [9]. In addition, other inflammatory mediators such as interferons e.g., IFN-α, and IFN-γ, interleukins e.g., IL-1β, IL-12, IL-18, tumor necrosis factor-α (TNF- α), and chemokines e.g., CCL2, CXCL10 have been reported in severely ill patients. These mediators represent the corner stone in developing cytokine storm that results in uncontrolled systemic inflammatory reaction with subsequent acute respiratory distress syndrome (ARDS), multiple organ failure and eventually death [10]. This mechanism of cell damage represents a target for already existing medications that modulate the immune response such as tocilizumab, monoclonal antibody against IL-6 receptors [11]. Based on its anti-inflammatory effects, colchicine has also gained attention to be utilized in the management of COVID-19 patient [12]. Colchicine is an alkaloid drug that is formed from a plant called "Colchicum autumnale", also named as "autumn crocus" [13]. Colchicine is used in many autoinflammatory conditions e.g., gout, familial Mediterranean fever, and Behçet's syndrome [14]. Colchicine exerts its anti-inflammatory effect through inhibition of formation of microtubules which is considered an essential step in several cellular processes such as division, signalling, and migration. Microtubule formation has been found to facilitate the invitro infection by coronavirus [15]. Also, colchicine affects the cytokine cascade by inhibiting IL-1β leading to reduction in neutrophils recruitment, free radicles production and inflammasome stimulation [13]. Moreover, it has been documented that colchicine has been used in cardiac conditions caused by viral infection e.g., myocarditis caused by CMV or EBV, interstitial pneumonia, pericarditis resulting from influenza B infection. Beside the fore mentioned effects of colchicine, its usage is considered safe and affordable with wide availability [16]. This raises the concerns about the effectiveness of colchicine in COVID-19 treatment and the possibility of providing an improvement of the clinical course of the disease.

In conclusion, colchicine could have an important role in the management of COVID-19. New randomized controlled clinical trials to assess the effectiveness of colchicine in the management of COVID-19 are strongly and urgently needed.

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