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Colchicine; An inflammasome inhibitor and a potential therapy in severe COVID19?

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Implication for health policy/practice/research/medical education
Inflammatory reactions are among the most adverse complications of COVID-19 patients. These reactions occur generally via inflammasomes. Inflammasomes are regulated by some proteins such as NLRP3. Colchicine is well-known drug which bars inflammasome formation by inhibiting NLRP3. In presented article we propose studying efficacy, adverse effects, and exact mechanism of action of colchicine in COVID-19 patients.

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COVID-19 have engaged more than 6.5 million people around the globe. This disease is responsible for the death of more than 385 394 people so far. The viral characteristics of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), including its genome sequence, have been known. However, understanding the immunopathogenesis mechanisms of this virus is under work. In several patients with severe COVID-19, evidences suggest destructive phenomena of cytokine storm, hyper-inflammation, severe neutrophilic inflammation, lymphocytosis, lymphopenia, T cell exhaustion, natural killer (NK) cells response impairment, disruption of IFN-mediated virus clearance mechanisms, and infiltration of macrophages and neutrophils into lung tissue. The ultimate result of all cases above is acute lung failure, acute respiratory distress, and dysfunction of vital organs such as the liver, kidneys, heart, and nerve damage (1,2). Inflammasomes are multi-synthetic cytosolic assemblages that come together in response to PAMPs (pathogen-associated molecular patterns) and cytosolic DAMPs (damage-associated molecular patterns), and their function is to produce active forms of cytokines interleukin 1 beta (IL-1β), IL-10, IL-18, and tumor necrosis factor α (TNFα). Inflammasomes are mainly regulated by NLRP1, NLRP3, NLRC4, NAIP, and AIM2 genes and some sensor proteins such as Pyrin in transcriptional level. In SARS-CoV-2, it has previously been shown that complex interaction of virus with the host immune system activates inflammasomes using structural and non-structural proteins. Hence, causes severe inflammation in various ways. The newest models of mature SARS-CoV-2 peptides' structures depict the role of the viral particles in inflammation (3). Colchicine has a variety of effects on the immune system. Inflammasome inhibition as an inflammatory stimulant, along with its effect on various regulators, has made colchicine an effective Inflammasome inhibitor (4-6). Colchicine is an anti-inflammatory drug that is documented to be effective in treating COVID19-. Hence, the study of its mechanism of action and other potential strategies to reduce severe inflammation is noteworthy. Colchicine is an inexpensive and readily available drug, considering that COVID-19 is distributed worldwide. Colchicine inhibits the polymerization of microtubules, thereby preventing chemotaxis and activation of the NLRP3 component of inflammasome complex (7). Both activities have the potential to treat COVID-19. Therefore, we recommend research to assess the effectiveness and safety of colchicine in reducing the manifestations of severe COVID-19 inflammation. Colchicine has outstanding anti-inflammatory effects and, most importantly, is able to inhibit inflammasome formation (8,9). It has been proven to be effective as a drug in some inflammatory disorders such as gout (10,11). Side effects of colchicine is dose-related. Further studies are required to evaluated the optimal dosage in COVID-19 patients (12). COVID19- is still a medical puzzle with many tabs. A one-dimensional approach to this disease increases the likelihood of error.

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So far, it is clear that uncontrolled inflammation is a serious consequence of some diseases such as COVID-19, and the purpose of using immunomodulatory and immunosuppressants is to curb this outcome. The exact mechanism of action, efficacy, and adverse effects of colchicine in COVID-19 patients, should be determined in the context of more fundamental studies and clinical trials.

Authors' contribution

Conceptualization: SB and MB; Validation: MB; Investigation: SB and MB; Resources: MB; Data Curation: MB; Writing—Original Draft Preparation: MB, MRMS, BK, EA and AH; Writing—Review and Editing: MB, MRMS, BK, EA and AH; Visualization: MB; Supervision: MB; Project Administration: MB; Funding Acquisition: MB.

Conflicts of interest

The authors declare no conflict of interest.

Ethical issues

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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