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LETTER TO THE EDITOR

- 108 Can hydroxychloroquine be used for COVID-19-induced arthritis? A debatable hypothesis

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Can hydroxychloroquine be used for COVID-19-induced arthritis? A debatable hypothesis

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Abstract

Hydroxychloroquine (HCQ) is a known disease-modifying antirheumatic drug for rheumatoid arthritis. It is also being used in viral arthritis on many occasions. HCQ is also being used to treat coronavirus disease 2019, but the results are not satisfactory. HCQ has been shown to have antiviral effects. In this context, we have a hypothesis that HCQ may be used as a treatment option in post-coronavirus disease 2019 arthritis.

Key Words: COVID-19; Arthritis; Hydroxychloroquine; DMARDS; SARS-CoV-2; Post-COVID-19 arthritis

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Core Tip: Hydroxychloroquine is a known disease-modifying antirheumatic drug and has antiviral properties. It had previously been used to treat viral arthritis. In this letter, using future research questions in the context of the evidence in the literature we debate whether hydroxychloroquine can be used in post-coronavirus disease 2019 arthritis.

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TO THE EDITOR

We read with interest the article by Bajpai *et al*[1] where they presented 'for' and 'against' discussion regarding hydroxychloroquine (HCQ) in coronavirus disease 2019

(COVID-19). Severe acute respiratory syndrome coronavirus 2 is the causative agent of COVID-19 infection. Hydroxychloroquine is used to treat viral arthritis. In contrast, HCQ alone or in combination is not suitable for management of COVID-19[1]. Here, we highlighted the important issue of post-COVID-19 arthritis and its treatment with HCQ and further add to the 'for' and 'against' discussion.

COVID-19 is currently present at an endemic level through its acute and long-term consequences, even though its long-term effects have not been fully explored. The spectrum of involvement includes every system of the human body and can range from asymptomatic infection to fulminant systemic inflammatory response syndrome leading to death. Less has been known regarding the causal relationship between COVID-19 and inflammatory arthritis (acute or chronic) due to the scarcity of evidence in the literature. A review article by Conway *et al*[2] reported nine arthritis cases associated with COVID-19, but causality could not be drawn. From earlier studies exploring the pathway of development of arthritis associated with viral disease, three possible ways were determined: (1) Direct viral pathology; (2) immune complex-mediated inflammation; and (3) immune activation[3-9]. These mechanisms are likely the modes of development of arthritis in COVID-19.

Respiratory droplets are the primary mode of transmission of severe acute respiratory syndrome coronavirus 2. Upon transmission, the viral particles attach to the respiratory epithelium by high-affinity interactions of the spike protein with the angiotensin-converting enzyme 2 (ACE-2) receptor on epithelial cells. After binding to ACE-2, severe acute respiratory syndrome coronavirus 2 can enter the cells by endocytosis mechanism or through the plasma membrane. Synovial cells, cartilage, and fibroblasts express ACE-2 receptors and transmembrane serine protease 2, which help the virus to enter the cell. ACE-2 upregulation is also observed in inflamed rheumatoid arthritis synovial tissue.

HCQ, a less toxic derivative of chloroquine (a derivative of alkaloid quinine), is widely used by rheumatologists as a disease-modifying antirheumatic drug. It is currently under study to explore its role in preventing and treating COVID-19. The drug has been postulated to hinder viral entry, but the mechanism is still not completely understood. Several mechanisms have been proposed for the mechanism of antiviral action of HCQ. It blocks acidification of endosomes, interferes with the endocytosis of the virus and glycosylation of ACE-2 receptors or viral proteins by direct binding, sequesters metals, and exerts immunomodulation[10].

HCQ, apart from having antiviral effects, is also used as a disease-modifying antirheumatic drug for arthritis. HCQ has been previously used in Chikungunya arthritis (viral arthritis)[11]. Chikungunya is also known to exacerbate symptoms of rheumatic disease[11]. Furthermore, COVID-19 is a viral infection that has the potential to cause post-COVID-19 arthritis. There is also cross-talk exists between rheumatoid arthritis and COVID-19[12]. HCQ is used in rheumatoid arthritis as a disease-modifying antirheumatic drug. In such a context, our hypothesis emerged. However, the available evidence is scarce and unconvincing to definitely advise the use of HCQ for Post-COVID-19 arthritis. Further research is crucial and essential.

FOOTNOTES

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