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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. On the other hand, it is also being used in viral arthritis on many occasions. HCQ is also being used in coronavirus disease 2019 (COVID-19) but the results are not very satisfactory. HCQ has been also shown to have antiviral effects. In this context, we have our hypothesis on whether HCQ can be used in post-COVID-19 arthritis or not.

TO THE EDITOR

We read with interest the article by Bajpai *et al*^[1] where they have shown 'for' and 'against' discussion regarding Hydroxychloroquine (HCQ) in Coronavirus diseases (COVID-19). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the COVID-19 infection and Hydroxychloroquine is also used in viral arthritis. On the other hand, HCQ alone or with combination is not suitable for management for COVID-19^[1]. Here we would like to highlight the important issue of post-Covid arthritis and its treatment with HCQ. We would like to put this hypothesis in the light of available literature and furthermore would add 'for' and 'against' discussion on it.

COVID-19 Lingers globally at present at an endemic level through its acute and long-term consequences; though its long-term effects have not been fully explored. The spectrum of involvement expands through 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 literature; a review article by Conway *et al*^[2] reported 9 (nine) such cases associated with COVID-19 but causality couldn't be drawn. From earlier studies exploring the pathway of development of arthritis associated with viral disease three possible ways could be determined which also can be considered as the modes of development of arthritis in COVID-19 disease, they are: Direct viral pathology; immune complex-mediated inflammation and lastly immune activation^[3-9].

Respiratory droplets are the primary way of transmission of SARS-CoV-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, SARS-CoV-2 can enter the cells by endocytosis mechanism or through the plasma membrane. Synovial cells, cartilage, and fibroblasts have been seen to 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.

Hydroxychloroquine (HCQ); a less toxic derivative of chloroquine (a derivative of alkaloid quinine); which is widely being used by rheumatologists as a Disease-Modifying Antirheumatic Drug (DMARDs); is currently under study to explore its role in preventing and treatment of COVID-19 disease. The drug has been postulated to hinder viral entry but the progression is still not completely understood and not defined properly. There are several mechanisms have been proposed for the mechanism of antiviral action of HCQ. It blocks acidification of endosomes; interferes with the endocytosis of virus and glycosylation of ACE2 receptors or viral proteins by direct binding; it also sequesters metals, and exerts immunomodulation^[10].

HCQ, apart from having antiviral effects, is also used as a DMARDs 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, it has the potential to cause post-Covid arthritis. There is also cross-talk exists between Rheumatoid arthritis (RA) and COVID-19^[12]. HCQ is used in RA as a DMARD. In such a context, our hypothesis emerged. But the available evidence is little and not so convincing to advise HCQ for Post-Covid arthritis. Further research is crucial and essential to confirm it.

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