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LETTER TO THE EDITOR

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

Swarnakar R, Roy SS, Yadav SL

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Peer Reviewer of *World Journal of Experimental Medicine*, Azzam A Maghazachi, Professor, Department of Clinical Sciences, College of Medicine, Sharjah Institute for Medical Research, University of Sharjah, Sharjah, United Arabs Emirates. amagazachi@sharjah.ac.ae

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

Raktim Swarnakar, Sankha Subhra Roy, Shiv Lal Yadav

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Raktim Swarnakar, Sankha Subhra Roy, Shiv Lal Yadav, Department of Physical Medicine and Rehabilitation, All India Institute of Medical Sciences, New Delhi 110029, Delhi, India

Corresponding author: Raktim Swarnakar, MBBS, MD, Doctor, Department of Physical Medicine and Rehabilitation, All India Institute of Medical Sciences, New Delhi 110029, Delhi, India. raktimswarnakar@hotmail.com

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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Country/Territory of origin: India

ORCID number: Raktim Swarnakar [0000-0002-7221-2825](https://orcid.org/0000-0002-7221-2825).

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REFERENCES

- 1 **Bajpai J**, Pradhan A, Verma AK, Kant S. Use of hydroxychloroquine and azithromycin combination to treat the COVID-19 infection. *World J Exp Med* 2022; **12**: 44-52 [PMID: [35765514](https://pubmed.ncbi.nlm.nih.gov/35765514/) DOI: [10.5493/wjem.v12.i3.44](https://doi.org/10.5493/wjem.v12.i3.44)]
- 2 **Conway R**, Konig MF, Graef ER, Webb K, Yazdany J, Kim AHJ. Inflammatory arthritis in patients with COVID-19.

- Transl Res* 2021; **232**: 49-59 [PMID: 33626415 DOI: 10.1016/j.trsl.2021.02.010]
- 3 **Fraser JR**, Cunningham AL, Hayes K, Leach R, Lunt R. Rubella arthritis in adults. Isolation of virus, cytology and other aspects of the synovial reaction. *Clin Exp Rheumatol* 1983; **1**: 287-293 [PMID: 6398166]
 - 4 **Lennerz C**, Madry H, Ehlhardt S, Venzke T, Zang KD, Mehraein Y. Parvovirus B19-related chronic monoarthritis: immunohistochemical detection of virus-positive lymphocytes within the synovial tissue compartment: two reported cases. *Clin Rheumatol* 2004; **23**: 59-62 [PMID: 14749987 DOI: 10.1007/s10067-003-0800-8]
 - 5 **Kujala G**, Newman JH. Isolation of echovirus type 11 from synovial fluid in acute monocytic arthritis. *Arthritis Rheum* 1985; **28**: 98-99 [PMID: 3966942 DOI: 10.1002/art.1780280116]
 - 6 **Matava MJ**, Horgan M. Serial quantification of the human immunodeficiency virus in an arthroscopic effluent. *Arthroscopy* 1997; **13**: 739-742 [PMID: 9442328 DOI: 10.1016/s0749-8063(97)90010-4]
 - 7 **Withrington RH**, Cornes P, Harris JR, Seifert MH, Berrie E, Taylor-Robinson D, Jeffries DJ. Isolation of human immunodeficiency virus from synovial fluid of a patient with reactive arthritis. *Br Med J (Clin Res Ed)* 1987; **294**: 484 [PMID: 3103739 DOI: 10.1136/bmj.294.6570.484]
 - 8 **Soden M**, Vasudevan H, Roberts B, Coelen R, Hamlin G, Vasudevan S, La Brooy J. Detection of viral ribonucleic acid and histologic analysis of inflamed synovium in Ross River virus infection. *Arthritis Rheum* 2000; **43**: 365-369 [PMID: 10693876 DOI: 10.1002/1529-0131(200002)43:2<365::AID-ANR16>3.0.CO;2-E]
 - 9 **Hoarau JJ**, Jaffar Bandjee MC, Krejbich Trotot P, Das T, Li-Pat-Yuen G, Dassa B, Denizot M, Guichard E, Ribera A, Henni T, Tallet F, Moiton MP, Gauzère BA, Bruniquet S, Jaffar Bandjee Z, Morbidelli P, Martigny G, Jolivet M, Gay F, Grandadam M, Tolou H, Vieillard V, Debré P, Autran B, Gasque P. Persistent chronic inflammation and infection by Chikungunya arthritogenic alphavirus in spite of a robust host immune response. *J Immunol* 2010; **184**: 5914-5927 [PMID: 20404278 DOI: 10.4049/jimmunol.0900255]
 - 10 **Faraone I**, Labanca F, Ponticelli M, De Tommasi N, Milella L. Recent Clinical and Preclinical Studies of Hydroxychloroquine on RNA Viruses and Chronic Diseases: A Systematic Review. *Molecules* 2020; **25** [PMID: 33202656 DOI: 10.3390/molecules25225318]
 - 11 **Pathak H**, Mohan MC, Ravindran V. Chikungunya arthritis. *Clin Med (Lond)* 2019; **19**: 381-385 [PMID: 31530685 DOI: 10.7861/clinmed.2019-0035]
 - 12 **Dewanjee S**, Kandimalla R, Kalra RS, Valupadas C, Vallamkondu J, Kolli V, Dey Ray S, Reddy AP, Reddy PH. COVID-19 and Rheumatoid Arthritis Crosstalk: Emerging Association, Therapeutic Options and Challenges. *Cells* 2021; **10** [PMID: 34943795 DOI: 10.3390/cells10123291]



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