



## Coronavirus disease 2019 (COVID-19) and anti-rheumatic drugs

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To the Editor,

Current pandemic of coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Despite drastic containment measures, the COVID-19 outbreak has taken lives of more than 12,000 people worldwide, with the number of those contracting the virus surpassing 300,000 (as of March 22, 2020) [1]. The seriousness of the situation necessitates urgent multidisciplinary strategy to contain the spread of the disease and prevent its complications.

The affection of the lower airways in severe COVID-19 is driven by uncontrolled immune-mediated inflammatory response. T lymphocytes are the main target cells in severe acute respiratory syndrome (SARS) due to COVID-19, triggering cytokine storm with subsequent exhaustion of immune response [2, 3]. Importantly, there is no association between the viral load and severity of the disease [4]. The cascade of the disease pathways is reminiscent of systemic immune disturbances, particularly those in severe rheumatic flare. Based on the current knowledge of COVID-19 pathophysiology and clinical manifestations, the rationale for searching specific antivirals along with immune-modulating drugs is justifiable. A quick search through the US National Library of Medicine Clinical Trials registry (<https://clinicaltrials.gov/>) and the Chinese Clinical Trial Registry (<https://www.chictr.org.cn>) may help retrieve links to studies of anti-rheumatic drugs in COVID-19. Ongoing research brings about hope for developing evidence-based anti-rheumatic therapies for the viral disease.

Systemic corticosteroids (CS) are known to potently dampen immune inflammation. Like in inflammatory rheumatic diseases, CS might serve as a “bridge” to specific efficient antiviral therapy for COVID-19. Despite the common

fears of the virus replication, provisional recommendations for managing excessive inflammatory response in COVID-19 include intravenous CS [5]. The World Health Organization (WHO), however, recommends to avoid routine administration of systemic CS for the treatment of viral pneumonia outside clinical trials [6].

Chloroquine (CQ) and its less toxic derivative hydroxychloroquine (HCQ) are well known for their immunomodulating effects in rheumatology. For decades, these drugs have been used for the treatment of systemic lupus erythematosus and rheumatoid arthritis. The justification for their use in COVID-19 is largely based on the knowledge of their intracellular action [7]. These antimalarial drugs may disrupt the virus replication and subsequent cytokine storm in severe COVID-19 [8, 9]. CQ has proved efficient against the virus in COVID-19 pneumonia in Chinese clinical trials, justifying the inclusion of the drug in the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 [10]. An open-label non-randomized clinical trial by Gauret et al. showed that HCQ reduces viral load in most COVID-19 patients and that its efficacy is enhanced in combination with azithromycin [11]. HCQ low costs and relative safety profile may secure its place in the strategy against COVID-19 [12].

Interestingly, interleukin(IL)-6 levels are significantly elevated in severe COVID-19, suggesting its crucial role in cytokine storm and predicting adverse outcomes [13, 14]. IL-6 levels are associated with SARS-CoV-2 viral load [15]. Blocking IL-6 receptor might be a promising strategy in the disease management. Preliminary evidence from a small uncontrolled trial in China proves that tocilizumab in addition to routine therapy is effective for decreasing C-reactive protein levels and alleviating symptoms. Tocilizumab therapy is listed in the recommendations for severe COVID-19 management by the National Institute for the Infectious Diseases ‘Lazzaro Spallanzani’ [5].

The recent advances in the understanding of COVID-19 have pointed to the similarities of the cytokine storm syndromes in this viral disease and inflammatory rheumatic disorders, justifying the use of anti-rheumatic drugs in both

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conditions. Rheumatologists should share their experience with managing patients with rheumatic disorders and join the global multidisciplinary fight against COVID-19.

## Compliance with ethical standards

**Conflict of interest** Tsvetoslav Georgiev declares that he has no conflict of interest.

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