The coronavirus disease 2019 (COVID-19) pandemic has created a global public health crisis and severe economic disruption. There are currently no effective therapies to prevent, treat, or cure COVID-19. To meet this need, the scientific community has mobilized to develop vaccines and drugs to prevent and treat COVID-19. Trials are underway to assess the effectiveness of existing drugs that hold promise in treating COVID-19. While the results of these trials are eagerly awaited, the US Food and Drug Administration recently authorized use of chloroquine and hydroxychloroquine for emergency treatment of COVID-19.

In the US, chloroquine is used predominantly to treat infectious diseases, such as malaria. Its less-toxic metabolite, hydroxychloroquine, is prescribed for lupus, rheumatoid arthritis, and other autoimmune diseases. Indeed, hydroxychloroquine has long been a mainstay of lupus treatment, and it is the only drug shown to prevent progression to serious end-organ damage.

Lupus is a complex autoimmune disease that predominantly affects young women. The prevalence of lupus is higher and the severity greater among individuals from lower socioeconomic strata, African Americans, Hispanic Americans, and Asian Americans. Clinical features range from mild joint and skin involvement to life-threatening renal, hematologic, and/or central nervous system disease. Half of patients with lupus develop nephritis, the most common cause of morbidity and mortality. Patients with lupus who are impoverished and/or members of racial/ethnic minorities experience worse outcomes and increased mortality.

Hydroxychloroquine is recommended for all patients with lupus, especially those with no contraindication such as pregnancy. It relieves constitutional, musculoskeletal, and mucocutaneous manifestations and decreases thrombotic events, organ damage, and mortality. Hydroxychloroquine helps maintain disease remission and prevent flares. Among patients with lupus that is not organ threatening, 80% achieve remission with hydroxychloroquine and may sustain it with this therapy for long periods.

Although there is no rigorous scientific evidence supporting the use of hydroxychloroquine in COVID-19 as of early April 2020, consumers are stockpiling the drug not only for treatment but also prophylaxis prompted by media reports of possible efficacy. A rationale for hydroxychloroquine use in COVID-19 is based on in vitro studies showing that chloroquine inhibits virus replication. Because hydroxychloroquine and chloroquine may have in vivo antiviral and anti-inflammatory effects, they offer a potential means to mitigate COVID-19.

A recent small (n = 36), open-label nonrandomized trial in France suggested that therapy with hydroxychloroquine and azithromycin decreased viral load and replication, garnering significant media attention. However, randomized clinical trials are required to assess the efficacy and safety of hydroxychloroquine as prophylaxis or treatment for COVID-19. The FDA has authorized its use for treatment of patients hospitalized with COVID-19 but not for prophylaxis. President Trump has touted hydroxychloroquine therapy, despite very limited evidence of efficacy.

Since being prominently featured in the press and on social media as a potential COVID-19 therapy, demand for hydroxychloroquine has exploded and a shortage has ensued. Some physicians are prescribing it for prophylaxis as well as outpatient treatment of COVID-19, often along with azithromycin. Some health care workers are taking it as prophylaxis without any evidence to support this use.
However, if these uses of hydroxychloroquine to prevent and treat COVID-19 cause pharmacies to develop shortages of this drug, patients with lupus will find it difficult, if not impossible, to fill their routine hydroxychloroquine prescriptions. The American Society of Health-System Pharmacists has already confirmed shortages of hydroxychloroquine. Prior to COVID-19, many patients with lupus who have low incomes or limited prescription drug coverage found it difficult to pay for a 90-day supply and thus relied on monthly refills. Without their hydroxychloroquine refills, many will experience flare-ups and may develop irreversible organ damage.7

The potential misuse of hydroxychloroquine during the COVID-19 pandemic poses serious risks to patients with lupus who are socioeconomically vulnerable. Pharmacy shortages could lead to a black market for the drug, rendering it unaffordable for many patients with lupus. A black market for unsafe, counterfeit hydroxychloroquine could develop. Expedited FDA approval of hydroxychloroquine for COVID-19 could lead to a scenario similar to colchicine rebranding. In that case, the FDA granted exclusive rights to a single company to market the medication for all indications, and prices immediately increased nearly 30-fold. For patients with lupus, widespread unemployment, decreased financial resources, and loss of employer-sponsored insurance resulting from COVID-19 may make hydroxychloroquine unaffordable, even if it is available.

Although large pharmaceutical companies have committed to produce ample supplies of chloroquine and hydroxychloroquine, their timeline is uncertain, and these threats remain. As we have learned from consumer behavior with toilet paper, hand sanitizers, and masks during the COVID-19 crisis, even as the supply of hydroxychloroquine increases, barriers for patients with lupus who are vulnerable may persist. Stockpiling of hydroxychloroquine to prevent or treat COVID-19, despite very limited evidence of benefit, thus exposes these patients to enormous risks.

Maintaining remission in patients with lupus who are immunosuppressed is particularly important, given their increased vulnerability to COVID-19 and its most severe complications. Patients with lupus flare-ups will likely need systemic glucocorticoids or other immunosuppressive medications, further increasing their risk of infection and transmission of COVID-19 to others. Physicians must therefore prescribe hydroxychloroquine responsibly, if at all, when treating patients with COVID-19. Furthermore, policymakers should develop regulations to preserve access to an adequate supply of this lifesaving medication for patients with lupus and other autoimmune diseases.

ARTICLE INFORMATION

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REFERENCES

1. Carter EE, Barr SG, Clarke AE. The global burden of SLE: prevalence, health disparities and socioeconomic impact. *Nat Rev Rheumatol*. 2016;12(10):605-620. doi:10.1038/nrrheum.2016.137

2. Ruiz-Irastorza G, Ramos-Casals M, Brito-Zeron P, Khamashta MA. Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: a systematic review. *Ann Rheum Dis*. 2010;69(1):20-28. doi:10.1136/ard.2008.101766

3. Colson P, Rolain JM, Raoult D. Chloroquine for the 2019 novel coronavirus SARS-CoV-2. *Int J Antimicrob Agents*. 2020;55(3):105923. doi:10.1016/j.ijantimicag.2020.105923

4. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020;105949. doi:10.1016/j.ijantimicag.2020.105949
Multicenter Collaboration Group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for Chloroquine in the Treatment of Novel Coronavirus Pneumonia. [Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia]. Zhonghua Jie He He Hu Xi Za Zhao. 2020;43(0):E019.

Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends. 2020;14(1):72-73. doi:10.5582/bst.2020.01047

Canadian Hydroxychloroquine Study Group. A randomized study of the effect of withdrawing hydroxychloroquine sulfate in systemic lupus erythematosus. N Engl J Med. 1991;324(3):150-154. doi:10.1056/NEJM199101173240303