

LETTER

The impact of hydroxychloroquine shortages on patients with dermatological conditions during COVID-19 pandemic

Dear Editor,

In the midst of the COVID-19 pandemic, the Food and Drug Administration (FDA) approved the emergency use of hydroxychloroquine (HCQS), stating, "the known and potential benefits of chloroquine phosphate and hydroxychloroquine sulfate when used to treat COVID-19 outweigh the known and potential risks of such products."¹ On March 19, 2020, the President of the United States, Donald Trump, also stated that HCQS could be a "game-changer" for people with coronavirus without substantial evidence of the drug's efficacy, which led to increased purchasing of nonprescribed HCQS by the public and physicians for personal use, concerns regarding drug supply, and pharmacy shortages.^{2,3}

While recent reports have described the potential consequences of a HCQS shortage on patients with systemic lupus erythematosus (SLE),^{2,4} a shortage of HCQS may also affect patients with dermatological conditions such as dermatomyositis, sarcoidosis, lichen planus, granuloma annulare, polymorphous light eruption, and more, for which HCQS is prescribed under off-label indications (see Table 1) due to evidence of improvement after use of HCQS.⁴⁻⁶ For example,

Wolverton summarized the improvement of cutaneous sarcoidal granulomas in 17 patients after 4 to 12 weeks of treatment with HCQS 200 to 400 mg daily, among other dermatoses.⁵

On April 7, 2020, an article by the Consumer News and Business Channel reported a 21-year-old female with dermatomyositis, who has been using HCQS for the past 8 years to reduce her flare-ups, which would otherwise result in muscle weakness, pain, and her subsequent inability to complete instrumental activities of daily living including schoolwork.³ The author states that the patient, "describes the possibility that she won't be able to access the drug as 'terrifying.'" She only has a few more days before she runs out. Her pharmacy, which she contacted last week, is completely out of the medication."³

Fortunately, to help combat a potential shortage, on April 7, 2020, the FDA approved an Abbreviated New Drug Application (ANDA) for HCQS sulfate tablets for the treatment of uncomplicated malaria in adults with rheumatoid arthritis, SLE, and chronic discoid lupus erythematosus, while excluding the therapeutic and prophylactic use in COVID-19.¹ This approval will enable multiple suppliers to manufacture HCQS generically.

However, we continue to caution the hoarding of nonprescribed HCQS by the public, as present studies in the literature indicate conflicting findings regarding the efficacy of HCQS. The recent quasi-randomized comparative study by Barbosa et al, submitted to the *New England Journal of Medicine*, reported limited benefits and even the increased need for respiratory support escalation after administration of HCQS.⁷ In contrast, Gautret et al reported viral load reduction or disappearance in COVID-19 patients who received 600 mg of HCQS daily, with the effect reinforced upon the addition of azithromycin.⁸ Moreover, Conforti et al discuss the possible benefits of HCQS in combination with doxycycline due to doxycycline's well-defined antibiotic and anti-inflammatory properties demonstrated for several inflammatory airway diseases.⁹ Overall, due to conflicting evidence we hope that further studies and clinical trials with larger sample size will meticulously assess the efficacy of HCQS in COVID-19, as well as its efficacy in combination with azithromycin or doxycycline.


With inconclusive findings on the efficacy of HCQS in COVID-19, we emphasize that it is critical for pharmaceutical companies, with cooperation from the public, to ensure that HCQS is not dispensed without prescription, so that this antimalarial is available to patients with dermatological and other conditions for which HCQS has proven benefits. As dermatologists, we need to be aware of the possible

TABLE 1 FDA-approved and off-label antimalarial indications for dermatological conditions

| | |
|--|--|
| FDA approved: | |
| <ul style="list-style-type: none"> Lupus erythematosus | |
| Off-label: | |
| <i>Photosensitivity dermatoses:</i> | <i>Lymphocytic infiltrates:</i> |
| <ul style="list-style-type: none"> Dermatomyositis Chronic actinic dermatitis Polymorphous light eruption Porphyria cutanea tarda Solar urticaria | <ul style="list-style-type: none"> Lymphocytoma Lymphocytic infiltrate of Jessner |
| <i>Granulomatous dermatoses:</i> | <i>Other dermatoses:</i> |
| <ul style="list-style-type: none"> Sarcoidosis Granuloma annulare Interstitial granulomatous dermatitis Annular elastolytic giant cell granuloma | <ul style="list-style-type: none"> Morphea Oral lichen planus Psoriatic arthritis Urticarial vasculitis Chronic ulcerative stomatitis Reticular erythematous mucinosis |
| <i>Panniculitis:</i> | |
| <ul style="list-style-type: none"> Panniculitis Chronic erythema nodosum Lupus panniculitis | <ul style="list-style-type: none"> Pemphigus foliaceus Atopic dermatitis Localized scleroderma Follicular mucinosis |

Abbreviation: FDA, Food and Drug Administration.

HCQS shortages and the subsequent effects on our patients during the COVID-19 pandemic.

Monica Shah¹ 
Muskaan Sachdeva¹
Roni P. Dodiuk-Gad^{2,3,4}

¹Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

²Division of Dermatology, Department of Medicine, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

³Department of Dermatology, Ha'emek Medical Center, Afula, Israel

⁴Ruth and Bruce Rappaport Faculty of Medicine, Technion Institute of Technology, Haifa, Israel

Correspondence

Monica Shah, Faculty of Medicine, University of Toronto, 1 King's College Cir, Toronto, ON M5S 1A8, Canada.
Email: monica.shah@mail.utoronto.ca

ORCID

Monica Shah  <https://orcid.org/0000-0002-2024-3064>

REFERENCES

1. Coronavirus disease 2019 (COVID-19). U.S. Food and Drug Administration. <https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19#new>. 2020. Accessed April 13, 2020.
2. Peschken CA. Possible Consequences of a Shortage of Hydroxychloroquine for Patients with Systemic Lupus Erythematosus amid the COVID-19 Pandemic. *J Rheumatol*. 2020;47. <https://doi.org/10.3899/jrheum.200395> [Epub ahead of print].
3. Farr C. Patients with autoimmune diseases are running out of hydroxychloroquine. CNBC. <https://www.cnbc.com/2020/04/07/patients-with-autoimmune-diseases-running-out-of-hydroxychloroquine.html>. 2020. Accessed April 13, 2020.
4. Jakhar D, Kaur I. Potential of chloroquine and hydroxychloroquine to treat COVID-19 causes fears of shortages among people with systemic lupus erythematosus. *Nat Med*. 2020;26:632. <https://doi.org/10.1038/s41591-020-0853-0>.
5. Wolverton S. *Comprehensive Dermatologic Drug Therapy*. 3rd ed. Edinburgh: Elsevier-Saunders; 2013:241-251.
6. Wallace D. The use of chloroquine and hydroxychloroquine for non-infectious conditions other than rheumatoid arthritis or lupus: a critical review. *Lupus*. 1996;5:59-64. <https://doi.org/10.1177/0961203396005001131>.
7. Barbosa J, Kaitis D, Freeman R, Le K, Lin X. Clinical outcomes of hydroxychloroquine in hospitalized patients with COVID-19: a quasi-randomized comparative study. *N Engl J Med*. 2020; In Review. <https://bibliovid.org/clinical-outcomes-of-hydroxychloroquine-in-hospitalized-patients-with-covid-19-a-302>. Accessed April 13, 2020.
8. 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. <https://doi.org/10.1016/j.ijantimicag.2020.105949> [Epub ahead of print].
9. Conforti C, Giuffrida R, Zalaudek I, Di Meo N. Doxycycline, a widely used antibiotic in dermatology with a possible anti-inflammatory action against IL-6 in COVID-19 outbreak. *Dermatol Ther*. 2020;33(4):e13437. <https://doi.org/10.1111/dth.13437>.