

Guiding Principles from the American College of Rheumatology for Scarce Resource Allocation During the COVID-19 Pandemic: The Case of Hydroxychloroquine

Background

Ethical principles must be balanced when making decisions about scarce resource allocation. In extreme circumstances, like the COVID-19 pandemic caused by the SARS-CoV-2 virus, the focus of medical care “shifts from the needs of the individual (ethical principle of autonomy) to the needs of the community as a whole (ethical principle of distributive justice)” (1) with the goal of achieving the greatest good for the greatest number of people.

Hydroxychloroquine (HCQ) is an essential medicine for patients with systemic lupus erythematosus (SLE). It is also a mainstay of therapy for many patients with rheumatoid arthritis. In the case of SLE, including pregnant women with SLE, “hydroxychloroquine is the cornerstone of medical therapy... It should be used in every patient unless there is a clear contraindication. It is the only medication shown to increase survival in lupus patients. It has been shown to reduce lupus flares and prevent organ damage including cardiovascular events (2).” Withdrawal of HCQ from SLE patients for as short as two weeks, even in those with previously clinically stable disease, is associated with flares (3).

Chloroquine and hydroxychloroquine, among other agents (4), have demonstrated antiviral activity against SARS-CoV-2 in tissue culture (5-7). These findings, as well as the relative tolerability of HCQ in patients taking the drug for FDA-approved indications, have raised interest in these agents as potential therapeutic options in the current COVID-19 pandemic.

A high-profile report by Gautret, *et al.* (8) describing the use of HCQ alone and in combination with azithromycin in patients with COVID-19 was made public 17 March 2020. HCQ and azithromycin were subsequently promulgated as therapeutic options for patients with COVID-19 by President Trump and other government officials starting with a press conference on 19 March 2020. Serious flaws in the methodology and interpretation of the data in the Gautret paper were quickly publicized (9).

Shortages of HCQ, a drug with relatively few regular manufacturers and a history of shortages and price spikes in the US, were noted before the press conference and became widely reported in the days that followed (10).

We offer the following recommendations regarding the allocation of HCQ during the COVID-19 pandemic. All recommendations are based on current knowledge and are subject to revision as circumstances evolve.

Recommendations:

- Every effort must be made to ensure an adequate supply of HCQ for all patients who need it. Efforts to increase production and distribution of HCQ for rheumatology patients, as well as patients with COVID-19 where indicated, should be supported. Protections on the supply of HCQ should include all aspects of the supply chain from manufacturer to wholesaler, wholesaler to pharmacy and final distribution to patients.
- Adequate supplies of HCQ should be allocated for patients with SLE, especially pregnant SLE patients and those in whom even brief drug holidays would be reasonably expected to cause a flare of their disease.
- In the case of COVID-19, allocation of adequate supplies of HCQ should be prioritized (but not limited) to support clinical trials designed to test the efficacy of HCQ as pre-exposure prophylaxis, post-exposure prophylaxis, and therapy both in mild-to-moderate as well as severe cases of COVID-19.
- While the Gautret study (8), owing to a number of serious flaws in its methods and data interpretation, does not provide a scientific justification for allocation of HCQ to COVID-19 patients, pre-clinical data demonstrating antiviral activity of HCQ in tissue culture combined with the urgent need for effective therapy against SARS-CoV-2, does justify expedited controlled trials in humans. Such trials should be carried out by experienced investigators equipped to generate and interpret reliable results while safeguarding patient safety and informed consent. The risk of adverse events (including QT prolongation) in critically ill COVID-19 patients receiving HCQ in combination with other drugs underscores the need for HCQ trials to take place in a controlled setting.
- Decisions about allocation of HCQ should be made locally, with input from experts, based on local conditions and calibrated over time as circumstances evolve. Decisions around allocation should not be made *ad hoc* by individual dispensing pharmacies acting in isolation.
- Decisions about allocation of HCQ, whenever possible, should incorporate recommendations from rheumatologists and rheumatology health professionals who are expert in the management of HCQ and rheumatologic conditions for which HCQ is FDA-approved.
- Rheumatologists and rheumatology health professionals, in shared decision making with a patient, may reasonably pursue HCQ dose reductions and extend HCQ dosing intervals tailored to an individual patient's needs when faced with HCQ shortages.
- A limit on HCQ refills to 30 days for patients prescribed HCQ prior to the COVID-19 pandemic is reasonable if local circumstances necessitate such action.
- Restricting new starts of HCQ in the outpatient setting, pending approval by a rheumatologist or rheumatology health professional, may be reasonable in settings where rheumatologists and rheumatology health professionals are available to fulfill this role. In cases where HCQ is prescribed for cutaneous manifestations of SLE, dermatologists or dermatology health professionals should also be allowed to approve new prescriptions for HCQ.

- During HCQ shortages we urge insurers to exempt rheumatology patients from prior authorization, step therapy protocols, and other utilization management practices so that they may more readily gain access to appropriate alternatives as determined by their rheumatologist or rheumatology health professional.
- Importation restrictions on HCQ should be relaxed during the COVID-19 pandemic to create alternative avenues for distribution of HCQ in the US.

To Be Avoided

- Unrestricted access to HCQ for COVID-19 prophylaxis in the absence of clinical trial data supporting its use is inappropriate.
- Pharmacy-level restrictions on new starts of HCQ for patients with SLE are inappropriate.
- Predatory price increases or cost-sharing requirements, especially during the COVID-19 pandemic, should be vigorously opposed by regulatory bodies.

References:

- (1) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2206420/>
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- (3) https://www.nejm.org/doi/10.1056/NEJM199101173240303?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200www.ncbi.nlm.nih.gov
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- (10) <https://www.washingtonpost.com/business/2020/03/20/hospitals-doctors-are-wiping-out-supplies-an-unproven-coronavirus-treatment/>