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Opinion

# Chloroquine and Hydroxychloroquine in the Management of Coronavirus: Cares and Challenges

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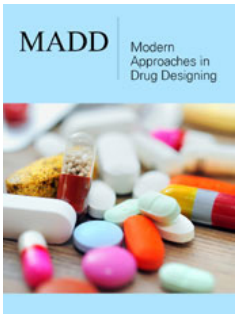


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## Opinion

The corona virus disease 2019 (COVID-19) pandemic has produced significant impacts on public health and global economy, due to hospitalizations, deaths, high complexity of clinical care and long quarantine periods required to control the spread of the causative virus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).As a result of the 2019 corona virus disease pandemic (COVID-19), there has been an urgent worldwide demand for treatments. Due to factors such as history of prescription for other infectious diseases, availability, and relatively low cost, the use of chloroquine (CQ) and hydroxyl chloroquine(HCQ) has been tested in vivo and in vitro for the ability to inhibit the causative virus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).

CQ and HCQ are synthetic anti malarials developed from the bark of cinchona (Rubiaceae), which are soluble in water (HCQ is more soluble because it possesses a hydroxyl group), are rapidly fast absorbed with a long plasma elimination half-life of 900 and 1300 hr, respectively. This leads to tissue bioaccumulation after chronic treatments. The cytochrome P450 complex is responsible for the metabolism of CQ and HCQ in the liver, with approximately 50% of metabolites excreted without modification by the kidneys. To be successful in replication, viruses need a host intracellular medium with a stable acidic pH in endosomes, lysosomes, and Golgi complex. The antiviral properties of CQ and HCQ are attributed to the accumulation of aminoquinolines that raise the pH of the medium in lysosomes and other intracellular acidic compartments and organelles.

It is important to emphasize that treatment ofCOVID-19 consists not only of inhibiting the viral replication of SARS-CoV-2, but also of controlling inflammatory processes by reducing the production of pro-inflammatory cytokines and other mediators. Regarding side effects, the main toxicological outcomes initiated by CQ and HCQ reported in the medical-scientific literature are related to retinopathy, neuromyopathy, and cardiomyopathy. In the retinal pigment epithelium, CQ and HCQ have an affinity for the melanin molecules, producing effects on macular cones (outside of the fovea).More specifically, the retinal pigmented cells react to the accumulation of external segments of the photoreceptors triggered by CQ and HCQ resulting in a decrease in phagocytic activity of lysosomes on the external segments of the photoreceptor, migrating to central and peripheral regions of the tissue and inducing epithelial a trophy with irreversible changes in its photoreceptors.

While controlled clinical studies are still lacking to epidemiologically clarify the incidence of cardiomyopathy and neuromyopathy, the toxicity produced in retinal cells was more comprehensively explored two aspects need to be considered when using CQ and HCQ to treat COVID-19:

a. it is a pandemic and, therefore, millions of people will receive treatment and,

b. the doses used in an acute approach to viral infection are often much higher when compared to utilization of CQ and HCQ for treatment of chronic rheumatic diseases. In addition, another very important epidemiological consideration is the fact that retinopathy is more common in Asian patients.

The main challenge is to consider as many epidemiological and clinical aspects as possible before starting treatment. In this context, it is important to know the history of previous (or ongoing) use of CQ and HCQ inpatients infected with malaria, amebiasis, or individuals with chronic diseases as rheumatoid arthritis and systemic lupus. As for possible drug interactions, the scientific literature describes that Kaolin clay and antacids interact with CQ and HCQ, which may reduce antiviral and anti-inflammatory activity. On the other hand, CQ and HCQ diminish the activity of antibiotics and immunosuppressants, such asampicillin and cyclosporin. Patients who are being treated with mefloquine are at increased risk of convulsions. There is no evidence that the use of CQ and HCQ has a preventive effect on the effects ofCOVID-19. Thus, clear information regarding the risk/benefit ratio of CQ and HCQ prescription needs to be shared among health professionals and extended to patients and the population. While researchers around the world are looking to develop target-specific drugs against the SARSCoV-2 virus, current approaches need to be grounded in practices of patient care minimizing risk by rigorous screening and measuring of doses.