Opinion

Hydroxychloroquine: a familiar agent to combat the pandemic of COVID-19

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Abstract

The emergence and pandemic spread of the novel SARS coronavirus 2, SARS-CoV-2, and the disease it causes, COVID-19, has sparked rapid research into the molecular mechanisms of the virus and potential therapeutic targets. Although strict quarantine is being employed by nations throughout the world, therapeutic agents to treat those affected and curtail the spread of infection are needed immediately. Hydroxychloroquine and chloroquine, biologically similar agents only differing by the presence of a hydroxyl group, have been indicated to have therapeutic potential through in vitro, animal, and human studies. Given hydroxychloroquine's superior efficacy in vitro for prophylaxis, it should be further explored as a prophylactic agent to prevent infection and spread, and immediately considered as a therapy for the treatment of COVID-19 at a dose guided by its other treatment indications and predictive preclinical modeling of 400 mg orally per day.

1. Introduction

The novel coronavirus, COVID-19, has taken the world by storm causing widespread quarantines and lockdowns of entire nations, actions not seen in over a century since the 1918 Spanish Influenza. The natural defense against an infectious pathogen is to avoid contracting the pathogen altogether through quarantine, a practice employed since antiquity (*1*). As world leaders allude to the promise of vaccines in a brief time period and the development of novel agents for treatment, perhaps we should examine whether already existing therapeutics are effective in treating people affected with COVID-19.

2. Supportive Evidence for Hydroxychloroquine

Researchers in China, the nation first affected by COVID-19, expeditiously assessed the potential use of already existing compounds in treating COVID-19. Hydroxychloroquine and chloroquine (non-hydroxylated compound) have demonstrated effective control of infection with COVID-19 in vitro (*2*). Hydroxychloroquine demonstrated comparable efficacy to chloroquine when used as a treatment against SARS-CoV-2 infection in vitro and in Vero cells, and was superior to chloroquine when used as pre-treatment prophylaxis (*3*). Impressive in vitro results conducted and published in rapid timeframes have sparked interest into the use of these compounds in the fight against COVID-19 infection, igniting a wave of international clinical trials and leading to the adoption of hydroxychloroquine and chloroquine into national guidelines in several countries including China, Korea, and Poland for the treatment of COVID-19 (*4*).

The potential use of chloroquine or hydroxychloroquine as an antiviral is not a novel concept. Chloroquine has demonstrated efficacy against SARS-CoV in vitro, against avian

influenza A H5N1 in mice, and against human coronavirus OC43 in newborn mice (*5,6,7*), demonstrated long before the emergence of the novel SARS-CoV-2.

Clinical evidence is also mounting as evidenced in a recent clinical study in February 2020, where Gao and colleagues published an interim report from clinical trials describing that chloroquine has demonstrated superior efficacy in the treatment of COVID-19 infection as seen in multiple disease parameters in humans, leading to a recommendation of its widespread use (*8*). This led to the adoption of hydroxychloroquine or chloroquine as a therapeutic agent for COVID-19 in the guidelines of several nations including China, Korea, Italy, and Poland (*4*). A clinical trial recently published from Marseille found hydroxychloroquine to be superior to standard of care in eradication of the virus, complemented by recent additional reports of encouraging results with hydroxychloroquine or chloroquine in news outlets (*9*).

3. Discussion

Given that hydroxychloroquine and chloroquine are among the most widely prescribed medications in the world, we can be confident about their safety. Of course with any therapeutic agent there are always risks of adverse effects, yet hydroxychloroquine and chloroquine are generally safe for short-term use. Recommended dosing regimens from recent literature, national guidelines, and individual hospital guidelines for COVID-19 have been similar to those currently used for malaria (*3,8)*. Given that hydroxychloroquine has demonstrated superior efficacy in vitro for the prevention of infection, it should be considered as a first-line agent against COVID-19 infection over chloroquine. Hydroxychloroquine should be utilized immediately given the low risks associated with treatment and be further explored as a therapeutic agent at a dose of 400 mg orally per day. Of particular interest would be further studies examining the

utility of hydroxychloroquine for prophylaxis against COVID-19 at a weekly dose of 400 mg orally given the long half-life (over 40 days), given its previous utility as a prophylactic agent against malaria infections, and promising in vitro results (*3,10*). Hydroxychloroquine taken at 400 mg orally per day during active infection may offer an avenue of infection control and treatment of affected individuals. Perhaps the answer to this once in a lifetime pandemic can be found from a dependable agent that has been used in the treatment of malaria for several decades and can be found readily throughout the world.

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