

Chloroquine: Can it be a Novel Drug for COVID-19

Abstract

Coronavirus disease 2019 (COVID-19) has been declared a pandemic by the World Health Organization. The United States Food and Drug Administration has not approved any drug or vaccine for the treatment of COVID-19; however, reports have emerged from different parts of the world about the potential therapeutic benefits of existing drugs. Chloroquine and phosphate hydroxychloroquine are the drugs currently in the limelight, and recently, the National Task Force for COVID-19 constituted by the Indian Council of Medical Research has recommended the use of antimalarial drug hydroxychloroquine for prophylaxis of severe acute respiratory syndrome-coronavirus 2 infection in selected high-risk individuals. This short write-up explores the potential efficacy and established safety of chloroquine in COVID-19.

Keywords: Chloroquine, coronavirus, coronavirus disease 2019, hydroxychloroquine

Introduction

It is a challenging time for the entire medical world to manage coronavirus disease 2019 (COVID-19), a respiratory illness caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) which is closely related to severe acute respiratory syndrome-CoV (SARS-CoV). This virus belongs to *Betacoronavirus* which also contains SARS-CoV and Middle East respiratory syndrome-CoV (MERS-CoV).^[1,2]

The treatment of the patients with COVID-19 is the major challenge as mortality ranges from 3% to 4% as compared to seasonal influenza (0.1%).^[3] More than 4,65,000 cases have now been reported to the World Health Organization (WHO), and more than 21,000 people have lost their lives as of March 27, 2020. The disease started in December 2019 in China and spread to 200 countries as of now. The number is increasing day by day. It has been declared a pandemic by the WHO.^[4] The therapeutic options being tried are based on the earlier experiences with other viral outbreaks, i.e. SARS/MERS as well as genomic sequence of the new virus. Many potential drugs including ribavirin, interferon, lopinavir–ritonavir, corticosteroids, penciclovir, nitazoxanide,

nafamostat, remdesivir, favipiravir, oseltamivir, azithromycin, baricitinib, and traditional Chinese medicine are being explored.^[5-8] However, as of now, there is no United States Food and Drug Administration-approved drug or vaccine available for COVID-19.^[9]

Chloroquine

An old drug with established safety and efficacy in malaria is being talked about so much so that it is going out of stock due to panic buying. Chloroquine, an antimalarial, antiamebic, immunomodulatory, and a potential broad-spectrum antiviral drug, is being reported to be effective in COVID-19. Chloroquine was discovered by Hans Andersag in 1934.^[10] Chloroquine phosphate is being recommended in malaria in chloroquine-sensitive *Plasmodium falciparum* malaria and is the first choice of drug in *Plasmodium vivax* malaria as per a national program in India. The recommended dose for treatment in malaria is 600 mg base (1000 mg salt) orally immediately, followed by 300 mg base (500 mg salt) orally at 6, 24, and 48 h. The total dose is 1500 mg base (2500 mg salt) over 3 days. The loading dose on day 1 is needed due to the large volume of distribution. The prophylactic dose is 500 mg weekly to be started 1 week before entering a malarious area and to continue 4 weeks after returning.^[2,11]

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**Dinesh Kumar Badyal^{1,2},
Rajiv Mahajan³**

Departments of ¹Pharmacology and ²Medical Education, CMCL-FAIMER Regional Institute, Christian Medical College, Ludhiana, ³Department of Pharmacology, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India

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Address for correspondence:

Dr. Dinesh Kumar Badyal,
Department of Pharmacology,
CMCL-FAIMER, Christian
Medical College,
Ludhiana - 141 008,
Punjab, India.
E-mail: dineshbadyal@gmail.
com

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Mechanism in Coronavirus Disease 2019

Chloroquine is extensively distributed in the entire body including lungs after oral administration. The main target cells for the SARS-CoV-2 are enterocytes and pneumocytes after it enters the body. After entry, the release of viral genome into the cytoplasm needs fusion of viral and cell membranes, and it attaches to these cells with the help of spike protein–host cell protein interaction. Chloroquine blocks virus infection by elevating endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of the virus. It is reported to act at virus entry and at postentry stages of the infection *in vitro* cells. Its anti-inflammatory and immunomodulatory action can add to its efficacy in COVID-19.^[5,6,12]

Studies in Coronavirus Disease 2019

It is reported to be effective in COVID-19-associated pneumonia inhibiting the exacerbation of pneumonia, earlier conversion to virus negative, and shortening the disease duration. However, this is based on the treatment of few hundred patients, and large controlled studies are needed to confirm the claims. Hydroxychloroquine, to chloroquine addition of beta-hydroxy chain, has fewer adverse effects, and less efficacy in malaria is being used in rheumatoid arthritis and systemic lupus erythematosus. It is also being explored on a similar basis for COVID-19.^[2,6,7,13,14] The Chinese Clinical Trial Registry has 506 studies registered on COVID-19, and out of these, 17 are on chloroquine and 7 are on hydroxychloroquine.^[15] Both chloroquine and hydroxychloroquine are 4-aminoquinolines and are in the National List of Essential Medicines of India.^[16] Due to its promising results, chloroquine has been included in guidelines for the diagnosis and treatment of COVID-19 (sixth edition) published by the National Health Commission of the People's Republic of China.^[17] The Central Drugs Standard Control Organization in India has invited applications in the vaccine/drug development, and these will be given high priority.^[18]

Role in Prevention

There is no conclusive evidence as of now about prophylactic value of chloroquine in COVID-19, although there are many queries by health-care workers to start chloroquine 500 mg weekly. In India, The National Task Force for COVID-19 constituted by the Indian Council of Medical Research has recommended the use of antimalarial drug hydroxychloroquine for prophylaxis of SARS-CoV-2 infection in selected high-risk individuals.^[19]

Safety of Chloroquine

Chloroquine is being used for more than 80 years as an inexpensive and safe drug. The safety profile is excellent and well established over time. Chloroquine can be prescribed to adults, children of all ages, pregnant women,

and nursing mothers. It has milder adverse effects when taken as prescribed. Milder and frequent adverse effects include gastrointestinal intolerance, i.e. nausea, vomiting, and epigastric pain. A higher dose can lead to retinal toxicity, seizures, pruritus, and photosensitivity.^[2,5,10,14] In 2014, Stevens–Johnson syndrome (SJS) was added as an adverse drug reaction into the prescribing information leaflet of chloroquine in India. SJS is a rare and serious disorder of the skin and mucous membranes.^[20]

Conclusion

A time-tested, established safe drug, chloroquine, is reported to be a promising drug for the treatment of COVID-19. However, accelerated studies involving large number of patients are required to confirm the efficacy to optimize its use in the international emergency situation due to COVID-19.

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Conflicts of interest

There are no conflicts of interest.

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