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A Perspective Approach Of Hydroxychloroquine In The Treatment for Covid-19

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ABSTRACT

Hydroxychloroquine is used in the treatment of malaria due to its pharmacological activity and with minimal adverse effects. Hydroxychloroquine is used in treatment of the diseases like rheumatoid arthritis and lupus erythematosus. In some countries, it is also indicated in the prevention or treatment of malaria. It has been developed in the 1950s from chloroquine, an old anti-malarial drug. COVID-19 is a highly contagious disease, transmitted through respiratory droplets by affected person through sneezing, coughing, talking, which also spread by touching a contaminated surface or may object. The person infected with the disease shows flu-like symptoms such as fever, muscle pain, cough and sore throat in five to six days after infection, while some patients may remain asymptomatic carriers. The disease further develops severe pneumonia in the patients. The mortality rate is high in patients with underlying conditions and those aged 60 years and above. This review complies about the mechanism, precautions, toxicity, ongoing trials of hydroxychloroquine and their medicinal usage.

Keywords: Chloroquine, Clinical trials, COVID-19, Hydroxychloroquine.

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INTRODUCTION

COVID-19 is a disease caused by coronavirus and it is proliferated very rapidly in the universe, with much incertitude about treatment and prevention. COVID-19, begins with respiratory symptoms like fever, body ache, eye irritation, coughing. COVID-19 progressively multiplied in the countries America, China, Italy, Spain, England, France, and India. In recent times, abounding trials delineating to regulate an adequate procedure for the remedy of COVID-19 [1].In populace, apparently high number of asymptomatic transporter are present and hence the fatality rate is exaggerated. A great accord of effort is continuing to find effective therapeutics and preventive measures against this transmissible virus with high mortality. So in that emergency, we need an efficient treatment for symptomatic patients and it also reduces the period of virus transference in the populace. Of the objective regimens, amino quinolones like chloroquine, hydroxychloroquine treatment is being contemplated. In the treatment of malaria with chloroquine phosphate so many clinical trials are available. In that the dose of 500mg/day was used to be efficient against in treating COVID-19 [2]. By *in vitro* studies, shows hydroxychloroquine produces the activity against antiSARS-CoV [3].The clinical safety of hydroxychloroquine is superior when compared to chloroquine and permits maximum daily dose on long-term treatment [4].

Chloroquine & Hydroxychloroquine

Chloroquine exhibits different types of mechanisms.

1. Chloroquine can prohibit initial accessible of virus into the cells by attaching to the surface of cell by the enzyme called angiotensin –converting enzyme 2.
2. Chloroquine acts by augmenting the pH subordinates the entry of virus causes deteriorate the early stages of virus replication.
3. Chloroquine also produces uncoating of virus, thus blocks the cell division.
4. Increase in pH affects the conformational changes of viral proteins like glycosyltransferases and proteases present in Golgi vesicles and endoplasmic reticulum get affected respectively.
5. Chloroquine interferes with processing of antigen cells, so that attaining an antirheumatic activity [5].

Hydroxychloroquine may have possible mechanisms are:

1. Hydroxychloroquine contains N-hydroxyethyl side chain leads to lesser adverse effects when compared to that of chloroquine possess N-diethyl group. Hydroxychloroquine causes rise in pH, produces anti-viral effects similarly to that of chloroquine.

2. Hydroxychloroquine reduces Toll-like receptors (TLRs) expression and signal transduction mediated by Toll-like receptors thereby it declines the formation of interleukin-6. Hence hydroxychloroquine produces anti-inflammatory effect.

The usage of hydroxychloroquine favored due to its lesser retinal toxicity and less availability of chloroquine than hydroxychloroquine in some countries.

FDA Emergency Use Authorization

- FDA is not approving chloroquine in the treatment of corona virus disease.
- EUA is aid the chloroquine availability during the COVID-19 pandemic treatment of the patients for whom not available for clinical trials, or participants is not feasible.
- EUA mentions the treatment is for adult patient's weighs above 50 kg are hospitalized with COVID-19 [6, 7].

Precautions

Patients administered with hydroxychloroquine will be often followed their hematological parameters, serum electrolytes, blood glucose, hepatic and renal functions. As these drugs are known to cause prolongation of QT interval, routine electrocardiogram is essential prior to starting these drugs.

Hydroxychloroquine and chloroquine work in a similar way as antimalarial medication with divergent therapeutic and toxic doses and produce a similar pattern of retinopathy. Hydroxychloroquine produces fewer ocular toxicity, because it does not able to crosses the blood-retinal barrier. In retina hydroxychloroquine produces noxious effects; it is associated by retinal pigment epithelium (RPE). In RPE drug attaches with melanin, it affects the retinal cells metabolism and produces adverse effects.

Ongoing trials on Hydroxychloroquine

The preliminary study in France evaluated the efficacy of HCQ in COVID-19 patients. There were 2 groups in this study, 26 patients received hydroxychloroquine (200mg*tid* for 10 days) and 16 patients received standard of care. Six hydroxychloroquine group patients lost follow-up due to early stoppage of treatment. Six patients in hydroxychloroquine group included azithromycin additionally (azithromycin - 500 mg on day 1, 250 mg once daily for next 4 days) to prevent bacterial superinfection. Result shows the virologicaly cured rate was significantly higher in hydroxychloroquine combined with azithromycin-treated patients comparing to the hydroxychloroquine only group or control group (100% vs. 57.1% vs. 12.5%, P = 0.001) [8].

In a study reported early findings on moreover 100 patients with chloroquine was significant to placebo in reducing pneumonia exacerbation, duration of illness and duration of clearance of virus

[9].This report must be viewed as extremely preliminary with minimal information regarding methodology and analysis of data provided. Even so, with these early results, chloroquine was included in treating COVID-19 pneumonia [10]. In another study have suggested that hydroxychloroquine, which has a similar mechanism of action as chloroquine, could be equally effective with a suggested dosage of 600 mg/day in order to reach serum concentrations of 1µg/ml [11, 12].

The World Health Organization (WHO) announced an international clinical trial called "Solidarity" to investigate the use of several medicines, including hydroxychloroquine, in the management of COVID-19.In addition, several independent trials are being conducted in parallel in different countries to find answers to many questions on the use of this medicine in COVID-19 as fast as possible.

Prophylaxis treatment against COVID-19

The various strategies for prevention of transmission and infection of this respiratory pathogen include:

1) Health promotion - non pharmacological interventions:

a. Isolation at home,
b. Voluntary quarantine at home,
c. Social distancing of entire population especially of the elderly and
d. Temporary closure of schools, universities and work places [13].

2) Specific protection through chemoprophylaxis or immunoprophylaxis which includes:

a. Antiviral agents
b. Chloroquine-Hydroxychloroquine
c. Vaccination.

CONCLUSION

This article is an overview of the emerging prophylaxis strategies about hydroxychloroquine under investigation against COVID-19.There are three major reasons for this: (i) hydroxychloroquine is likely to attenuate the severe progression of COVID-19 through inhibiting the cytokine storm by reducing CD154 expression in T cells (ii) hydroxychloroquine may confer a similar antiviral effect at both pre- and post- infection stages (iii) hydroxychloroquine has fewer side effects, is safe in pregnancy and is cheaper and more high availability. Given the fast-growing number of COVID-19 patients and the urgent need for effective and safe drugs in the clinic, it is more practical to identify reliable candidates by screening currently available drugs. We herein strongly urge that clinical trials are performed to assess the preventive effects of hydroxychloroquine on both

infection and malignant progression. Our medical and scientific community is working at full speed to find answers about potential solutions, including hydroxychloroquine and other medicines. We may start to have preliminary results from ongoing clinical studies in the coming weeks. It is important to act fast, but it is equally important to take all the necessary precautions to ensure patient safety.

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