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Editorial

Use of hydroxychloroquine for novel corona virus infection in India: is it ethically justifiable?

Ramesh Verma[1], Vinod Chayal[1], Meenakshi Kalhan[1]*, Rohit Dhaka[2], Ginni Agrawal[1], Piyush Jain[3], Tarun Singh[1]

[1]Department of Community Medicine, [3]Department of Forensic Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India
[2]Department of Community Medicine, ESIC Medical College & Hospital, Faridabad, Haryana, India

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***Correspondence:**
Dr. Meenakshi Kalhan,
E-mail: mkkalhan@gmail.com

Coronavirus disease is caused by a novel virus belonging to the family of corona viruses similar to severe acute respiratory syndrome (SARS) and name given to the novel virus as SARS Coronavirus- 2 (SARS-CoV-2) and the disease was named as COVID-19 on 11th February 2020 by World Health Organization (WHO).[1,2] First case of this infection was reported in December 2019 in Wuhan city of China and after that it spread globally.[3] On 30th January 2020, WHO declared this disease as Public Health Emergency of International Concern (PHEIC) and on 11th March 2020, WHO declared it as a pandemic when the infection was reported from all six WHO regions.[3,4]

The COVID-19 shows common symptoms like fever, malaise, dry cough, running nose, sneeze, sore throat, loss of smell, diarrhea as in other viral infections and the mean incubation period is 5.8 days (range 2-14 days).[1] Majority (80%) of infections result in mild symptoms while 15% patients show moderate symptoms like shortness of breath and need admission but 5% patients progress to viral pneumonia and multi-organ failure.[5] COVID-19 spreads from one person to another through small droplets or fomites produced when an infected person coughs, sneezes or even talks.[6,7] COVID-19 is highly contagious disease and till now, all over the world, more than 3.0 million are infected with case fatality rate (CFR) reported as 6.89 % while in India 28,500 cases have been reported with 3.27% CFR.[8,9] Till now, there is no vaccine or no specific antiviral treatment available in the world and the patients are being managed by giving symptomatic treatment, supportive care like oxygen and fluid therapy, and isolation or quarantine of the patients.[10]

In India, a national task force for COVID-19 constituted by Indian Council of Medical Research (ICMR) recommended the use of hydroxy-chloroquine (HCQ) in corona virus infected cases and advised it as a prophylaxis in asymptomatic household contacts of laboratory confirmed case and in asymptomatic health care workers involved in care of suspected or confirmed cases of COVID-19. The dose of HCQ is recommended as 400 mg BD for 1 day followed by 400 mg once in a week for 7 weeks.[11] On 31st March 2020, the Ministry of Health, Government of India approved the use of HCQ in combination with antibiotic (azithromycin) for patients with severe disease and requiring ICU management without considering its side effects like lowered blood pressure, ventricular arrhythmias, QT prolongation, other cardiac toxicity and may cause liver, muscle or nerve damage.[12] Sometimes retinal and psychiatric symptoms may also appear when taken in higher dose.

In India, HCQ primarily used to manage the malaria and available in tablet form and taken orally. HCQ has also immunomodulatory effect that reduces inflammatory pathway, which might reduce damage due to the exaggerated inflammatory response.[13] that's why HCQ is also prescribed in the treatment of rheumatoid arthritis, systemic lupus erythematous and Sjögren's syndrome. ICMR never advised in its advisory that before starting HCQ the person should fully be examined by physician and detailed history of any bleeding disorders, G6PD

deficiency disorder, COPD, heart diseases etc. should be taken. In India, on 29th March 2020, a doctor was died because of cardiac arrest after taking HCQ as prophylaxis. This unexpected death raised questions on India's policy to use an unproven drug as prophylaxis for healthcare workers and asymptomatic household contacts of COVID-19 patients.[14]

ICMR stated on 18 April 2020 that some of health care workers in India had taken HCQ themselves and they had shown side effects like nausea, vomiting, abdominal pain, hypoglycemia etc.[15] Ministry of Health and Family Welfare, Government of India issued an advisory on HCQ that it has been proven effective against the COVID-19 in vitro (laboratory) and *in vivo* studies.[16] But this statement is in fact not true because in India, the efficacy of HCQ in corona virus infection is carried out in vitro only and not in living organisms that's why question arises, is it ethically right to use high dose of HCQ in our country?

Very few recent studies conducted in vitro (petri dish or test tube) rather than in animals or humans and their findings have shown that both HCQ and chloroquine have antiviral properties against novel corona virus (COVID-19) but till date, no acute viral infection has been successfully treated by HCQ.[17,18] Marcia Frellick conducted a randomized controlled trial (RCT) on 150 adults COVID-19 hospitalized patients in China. He reported that HCQ does not clear the SARS-CoV-2 virus or relieve symptoms for COVID-19 patients in comparison to standard management alone and probably has got more side effects.[19]

According to a report, more deaths are being reported in USA among those patients who were given HCQ. National Institute of Health (NIH), USA stated that therapeutic or prophylaxis for COVID-19 currently are under trial and they have insufficient clinical data to either recommend or oppose using HCQ or chloroquine for treatment of Covid-19.[20] The Food and Drug Administration (FDA), USA warned against prescribing HCQ or chloroquine to treat COVID-19 patients when some serious side effects and deaths were reported. FDA also issued an advisory to medical professionals, in which they warned that they don't prescribe the drugs to treat the COVID-19 patient outside of a hospital.[21]

The researchers studied the pharmacokinetics properties of these two drugs (HCQ and CQ) and found out that these drugs interfere with the chemical environment of human cell membranes and blocked the virus from entering and multiplying inside the cells but scientists are of the view that a drug working *in vitro* does not always mean that it will definitely work inside the human body. In China also, they studied that chloroquine could inhibit SARS-CoV-2 *in vitro*. The research conducted in France, Brazil, China reported that HCQ neither reduced deaths nor admissions to intensive care unit and also failed to clear the coronavirus in COVID-19 patients. Another study from USA made public on April 16, 2020 analyzed medical records of 368 hospitalized patients with the coronavirus infection and reported that HCQ does not make any difference in the need for a breathing machine either.[22]

Many scientists from the all over the world think that more clinical trials are required to test the efficacy of HCQ against the corona virus before it is used and proven safe. The head of the US' National Institute of Allergy and Infectious Diseases, Mr Anthony Fauci said that evidence of efficacy of HCQ against COVID-19 is unreliable. He also quoted that "testing of HCQ was not done in a controlled clinical trial, so you can't really make any definitive statement about efficacy of this drug.[23]

In India, ICMR is carrying out an observational study on the impact of anti-malarial drug HCQ as a prophylactic and therapeutic drug among 480 COVID-19 patients and the study will take 2.5 months to be completed. ICMR stated that they cannot doing a trial because of insufficient evidence to conduct a trial in India.[24]

The health care professionals themselves should go through the available data from available literature and avoid misuse of HCQ for the treatment or prophylaxis of COVID-19 because in India, no authentic data are available to support the use of HCQ in treatment purpose or as a prophylaxis. In this time of crisis, it is our ethical and moral responsibility as the researcher to apprise the government that first of all, there is need to conduct randomized clinical trials in human beings to evaluate the safety, efficacy and dose of HCQ in COVID-19 patients and also trials are required whether the use of HCQ as a prophylaxis is beneficial or not before blanket recommendations are made.

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