

Hydroxy-Chloroquine - Prophylaxis For COVID-19

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Hydroxychloroquine, remains the widely used First Line Drug in many patients with rheumatologic conditions, such as rheumatoid arthritis and systemic lupus erythematosus. Recently, hydroxychloroquine attracted widespread interest as potential preventive therapy for coronavirus disease 2019.

Although the level of evidence in its favor is not sufficient but still in the light of current COVID 19 Pandemic, a declared Public Health Emergency, HCQs could find recommendation in India as well as world wide.

In India National Task Force for COVID 19 recommended hydroxychloroquine on the basis of In Vivo and Preclinical Data for its utility against SARS-CoV-2 Infection for the Prophylaxis of Health Care Workers and House Hold Contacts in Selected Cases only with caution and strict advisory for extensive reporting of ADRs countrywide on 22 March, 2020. (1)

Jia Liu *et al*, reported that hydroxychloroquine a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. (2)

The Met analysis of Meo, *et al* (3) reviewing in vitro studies, in vivo studies, original studies, clinical trials, and consensus reports published till date suggested that hydroxychloroquine have antiviral characteristics in vitro, and it has been demonstrated to limit the replication of SARS-CoV-2 virus in vitro. Further the said Met analysis also established one very interesting fact that COVID-19 infections are highly pandemic in countries where malaria is least pandemic and are least pandemic in nations where malaria is highly pandemic. Thereby, supporting the Hypothesis that these drugs (hydroxychloroquine and Chloroquine) have efficacy in the treatment of COVID-19.

Tripathy *et al* (4), suggested that CQ/HCQ has diverse modes of action, including alteration of the acidic environment inside lysosomes and late endosomes, preventing endocytosis, exosome release and

phagolysosomal fusion, and inhibition of the host cytokine storm. One or more diverse mechanisms might work against viral infections and reduce mortality against COVID 19. (4) The additional Mechanism proposed of HCQ in the form of its anti-viral, anti-inflammatory and anti-thrombotic drugs action may also result in anti COVID action. (5)

Shah *et al*. (6), in their Systematic Met analysis took, total of 45 articles including 5 (3 in vitro pre-clinical studies and 2 clinical opinions). The pre-clinical studies showed the prophylactic effects of CQ and HCQ against SARS-CoV-2. On the other hand, the clinical opinions advocated the prophylactic use of CQ and HCQ against COVID-19. However, no original clinical studies on the prophylactic role of CQ or HCQ on COVID-19 were available.

Although pre-clinical results are promising, to date there is a dearth of evidence to support the efficacy of CQ or HCQ in preventing COVID-19. Considering potential safety issues and the likelihood of imparting a false sense of security, prophylaxis with CQ or HCQ against COVID-19 needs to be thoroughly evaluated in observational studies or high-quality randomized controlled studies.

The clinical efficacy of CQ and HCQ in COVID-19 has yet to be proven with randomized controlled large studies, many of which are currently ongoing, also considering pharmacokinetics, optimal dosing regimen, therapeutic level and duration of treatment and taking into account patients with different severity degrees of disease. Presently, Revised advisory on the use of Hydroxychloroquine (HCQ) as prophylaxis for SARS-CoV-2 infection (in supersession of previous advisory dated 23rd March, 2020) has been issued by ICMR (7).

The safety data published till date by ICMR suggest that on assessment of HCQ prophylaxis among 1323 HCWs indicated mild adverse effects such as nausea (8.9%), abdominal pain (7.3%), vomiting (1.5%),

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hypoglycemia (1.7%) and cardio-vascular effects (1.9%).

However, as per the data from the Pharmacovigilance program of India, there have been 214 reported instances of adverse drug reactions associated with prophylactic HCQ use. Of these, 7 were serious individual case safety reports with prolongation of QT interval on ECG in 3 cases. (7).

The eligibility for the HCQ prophylaxis is Cat-1: Asymptomatic household contacts of laboratory confirmed cases. They shall receive HCQ 400 mg twice a day on Day 1, followed by 400 mg once weekly for next 3 weeks; to be taken with meals. Cat-2: All asymptomatic healthcare workers involved in containment and treatment of COVID-19 and asymptomatic healthcare workers working in non-COVID hospitals/ non-COVID areas of COVID hospitals/blocks and Asymptomatic frontline workers, such as surveillance workers deployed in containment zones and paramilitary/ police personnel involved in COVID-19 related activities. They shall receive HCQ 400 mg twice a day on Day 1, followed by 400 mg once weekly for next 7 weeks; to be taken with meals. (7)

The drug is contraindicated in persons with known case of Retinopathy, Hypersensitivity to HCQ or 4-aminoquinoline compounds, G6PD deficiency and Pre-existing cardiomyopathy and cardiac rhythm disorders (7)

ECG monitoring has been suggested by ICMR An ECG (with estimation of QT interval) may be done before prescribing HCQ prophylaxis. Further, An ECG should be done in case any new cardiovascular symptoms occurs (e.g., palpitations, chest pain syncope) during the course of prophylaxis. Also, it has been suggested that An ECG (with estimation of QT interval) may be done in those who are already on HCQ prophylaxis before continuing it beyond 8 weeks and One ECG should be done anytime during the course of prophylaxis. (7)

Further, ICMR is undoing metacentric study in India and it is expected that In India with, the start of ICMR-RUMC COVID 19 study for the assessment of HCQ prophylaxis for the health care workers, data shall contribute to the scientific literature evidence for or against HCQ for the Prophylaxis for COVID -19. infection.

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