



Offering Hydroxychloroquine Prophylaxis to High Risk Corona Warriors: Ongoing Debate

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Undoubtedly, it is high time to take up the COVID-19 challenge and act aptly and promptly to prevent the exponential spread of the highly transmissible novel corona virus worldwide to encounter this ongoing deadly healthcare crisis. SARS-CoV2 virus has been demonstrated to have high transmissibility with humans worldwide being clueless on how to manage its spread. As we are all aware, prevention is always better than cure. So shouldn't we proactively try to prevent the spread of novel corona virus by urgently putting in place interim guidelines for the monitored use of drugs having potential role as prophylactic agents against COVID-19 based on current available evidence rather than waiting for results of well controlled clinical trials on its role as prophylactic agent in preventing COVID infections as the delay could eventually prove counterproductive? With the novel coronavirus, we don't have the luxury of waiting for those big, randomized control trials. We need to visit the data we have and more necessarily act logically. Efforts on developing neutralizing antibodies, vaccines and also trials on use of antivirals are ongoing; however, the availability and cost of such therapies will be a major deterrent for a developing country like India with over 1.3 billion naïve population.

Hydroxychloroquine, an age old anti-malarial drug with known anti-inflammatory properties, used in rheumatoid arthritis, systemic lupus erythematosus, Q fever and porphyria cutanea tarda has shown promising results in treatment of COVID-19 infected patients either alone or in combination with Azithromycin [1]. Chloroquine has been shown to act as Zinc ionophore thereby enhancing the effects of zinc in preventing replication of RNA viruses [2].

Use of Zinc with pyrithione has been reported to inhibit replication of SARS-CoV [3,4]. Azithromycin is a macrolide antibiotic with well known anti-inflammatory properties and recently its combination with hydroxychloroquine has been shown to cure confirmed COVID-19 infected patients in 6 days in French study [1]. A few recent studies have, however, reported contradictory findings with use of hydroxychloroquine as a therapeutic drug in COVID-19 [5,6]. Currently, the scientific world is divided on the potential role of hydroxychloroquine in treatment of COVID-19 infection. Results of larger ongoing RCTs are awaited in order to get more evidence on this.

However, the prophylactic role of hydroxychloroquine deserves more attention because of its potential as a preventive strategy in the current pandemic. A study in 2005 had reported that chloroquine has strong antiviral effects on SARS-CoV infection of primate cells. These inhibitory effects were observed when the cells were treated with the drug either before or after exposure to the virus, suggesting both prophylactic and therapeutic advantage. In addition to the well-known functions of chloroquine such as elevations of endosomal pH, the drug appeared to interfere with terminal glycosylation of the cellular receptor, angiotensin-converting enzyme 2. This may negatively influence the virus-receptor binding and abrogate the infection, with further ramifications by the elevation of vesicular pH, resulting in the inhibition of infection and spread of SARS CoV at clinically admissible concentrations [7]. Similar observations have been reported by researchers wherein out of the armamentarium with high potential of role in treating COVID-19

infection, chloroquine has been documented to have inhibitory effects when the cells are treated with the drug even before exposure to the virus [8]. Such a prophylactic advantage of this drug may play a significant role in containment of COVID-19. Hydroxychloroquine has been reported to have similar efficacy profile as chloroquine but with better tolerability and safety profile. Hydroxychloroquine is also known to inhibit cytokine production and cytokine storm has been reported in SARS-CoV-2 infection, thereby suggesting its added advantage [9].

Based on these observations, it does seem rational to frame and urgently implement interim guidelines for monitored use hydroxychloroquine prophylaxis in high risk healthcare workers expected to come in contact with COVID-19 infected patients and asymptomatic contacts of confirmed COVID-19 cases to begin with and, if supported by further evidence, extend the prophylaxis to the general public. The same strategy has been followed by the premier scientific body of India: Indian Council of Medical Research (ICMR), New Delhi. ICMR had timely released its advisory on hydroxychloroquine use in health care workers involved in care of COVID-19 patients and suspects and asymptomatic household contacts of confirmed cases [10]. The advisory for use of hydroxychloroquine as a prophylactic drug has been updated recently based on promising data from three Indian studies as well as results of national pharmacovigilance program in which cardiac adverse events including prolonged QTc interval were rarely reported. Its use has now been extended to front-line corona warriors including surveillance workers deployed in containment zones and paramilitary/police personnel involved in COVID-19 related activities and duration of weekly use too has been extended beyond 8 weeks with strict ECG monitoring [11].

To conclude, Indian data as analyzed by ICMR, New Delhi is suggestive of potential role of hydroxychloroquine as prophylactic drug against SARS-CoV2. In addition, no significant serious adverse effects including cardiac events have been reported in last 8 weeks since the issue of first advisory. Data from therapeutic studies globally also suggests better results, if any, in those patients receiving hydroxychloroquine early in disease course when viral load is low. Based on all the aforementioned observations, it does seem prudent to permit a stringently monitored use of hydroxychloroquine (along with zinc) for frontline corona warriors as awaiting the results of large well designed RCTs on

its prophylactic role can prove counter-productive in the current pandemic with exponential rise in cases and deaths daily.

ICMR, New Delhi probably wants to act timely and not be sorry later.

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