

Can We Reduce the Risk or Severity of COVID-19 Disease? Pre-exposure Prophylaxis for COVID-19 Disease

COVID-19 is an aggressive infection that needs to be aggressively managed as the window period from infection to devastating complications is small. Doctors, nurses, paramedics, sanitary workers, housekeeping and cleaning personnel, all staff of organizations such as hospitals, blood banks, municipality corporation, institutes, media and police personnel and the elderly are vulnerable and most exposed to COVID-19 due to the nature of their work. While the world awaits the arrival of a vaccine, what can we do to stay safer? Several measures have been recommended, like wearing a mask, face shield, maintaining social distance (1–2 meters), frequent handwashing, regular use of sanitizer, avoiding touching of surfaces, **avoiding touching of the external surface of your mask, etc.**



Several medications have been used to treat corona infection; however, there is scant data with regard to prophylaxis. A couple of medications have shown some promise, which include hydroxychloroquine and recently ivermectin.

Pre-exposure Prophylaxis Using Hydroxychloroquine (HCQ)

Many researchers have found certain groups at high risk for COVID-19 disease, such as patients with hypertension, diabetes mellitus, obesity, kidney disease, asthma, chronic bronchitis with emphysema, chronic smokers, congestive heart failure, liver disease, malignancy, immune-compromised subjects, and elderly subjects >80 years of age.

In three randomized clinical trials of COVID-19, using HCQ for prophylaxis and therapeutics, there were no mortality and we did not find any significant safety issues.^{1–4}

Based on these observations, researchers have described a prophylactic regimen in the high-risk patients. They proposed a dose of 400 mg weekly based on malaria prophylaxis recommendations and may be continued for a month or longer depending on the degree of risk of viral exposure. They argue that this will allow individuals to resume work with some form of protection against COVID-19 and prevent high-risk individuals from getting infection from close contacts. It might attenuate the infection if it did occur.⁵

Using this approach, there are three controlled long-term trials in progress but the results will be delayed for quite some time. People are going back to work without any protection during the unlocking of restrictions. Pre-exposure prophylaxis is a practical way to fight the virus and with an objective to keep everybody safe. However, there are other studies which have not shown any proven benefit and recommended not to be prescribed due to the fear of cardiac toxicity. The Eastern Virginia Medical School (EVMS) critical care COVID-19 management protocols of Eastern do not recommend hydroxychloroquine prophylaxis.^{6,7}

Pre-exposure Prophylaxis Using Ivermectin

Ivermectin is another drug which has antiviral properties and appears to be effective in vitro and in vivo. It has a half-life of 12–36 hours in humans; and its metabolites may persist for up to 12 days. It has been attributed to high liposolubility of ivermectin. The pre-official release of a randomized controlled trial using ivermectin in two doses in primary contacts has shown significant difference. 58% of people who did not receive ivermectin went on to have symptoms and only 7% who took ivermectin progressed to have symptoms.

I commenced using ivermectin, doxycycline, zinc and colchicine in addition to other supportive measures for treatment of corona infection more than 6 months ago and found this very effective.

I am proposing quadruple therapy as prophylaxis against corona infection, on similar lines as proposed by an Australian gastroenterologist, Prof Thomas Borody, who is known for curing peptic ulcers with triple antibiotic therapy. Listening to one of his interviews, where he revealed that in South America, one block that received ivermectin combination prophylaxis did not contact corona infection, while others did. Quadruple therapy includes ivermectin 12 mg one dose, doxycycline 100 mg once daily for 4 days, zinc 50 mg once daily for 4 days and Vitamin D3 once a week. Ivermectin, doxycycline and zinc to be repeated every 14 days and Vitamin D3 every week with blood levels monitored after 8 weeks. The 14 days repetition for the medications is based on their complete excretion time from the body. These medicines act together to prevent the viral replication and also prevent from attaching to the ACE-2 receptors. This should offer some hope in protecting against corona virus or dampen the effects of corona virus infection. Ivermectin is being used in 3.7 billion people for intestinal parasites and is found relatively safe. These medications can be prescribed by any doctor and are readily available in pharmacies. I am hoping more and more doctors prescribe them to get control of this pandemic. I have feedback from many doctors who have found prophylaxis regime very encouraging. Please note, above recommendations are my opinion based on my reviewing many research papers and my own experience and feedback from doctors and completely independent of any organization.

Therapy with plasma or neutralizing monoclonal antibodies has been suggested, but their use has not been evaluated in randomized clinical trials yet.^{8–12}

Conclusion

There is an urgent need for active prophylaxis against COVID-19 when we reopen economy. Until we find a vaccine globally, pre-exposure prophylaxis for COVID-19 seems a better, logical way and may be feasible.

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References

1. Lofgren SM, Nicol MR, Bangdiwala AS, et al. Safety of hydroxychloroquine among outpatient clinical trial participants for COVID-19. *MedRxiv*. 2020. doi:10.1101/2020.07.16.20155531.
2. Sciascia S, Hunt BJ, Talavera-Garcia E, Lliso G, Khamashta MA, Cuadrado MJ. The impact of hydroxychloroquine treatment on pregnancy outcome in women with antiphospholipid antibodies. *Am J Obstet Gynecol*. 2016;214:273.e1–273.e8. doi:10.1016/j.ajog.2015.09.078.
3. Braun S, Ferner M, Kronfeld K, Griese M. Hydroxychloroquine in children with interstitial (diffuse parenchymal) lung diseases. *Pediatr Pulmonol*. 2015;50:410–419. doi:10.1002/ppul.23133.
4. Park JJH, Decloedt EH, Rayner CR, Cotton M, Mills EJ. Clinical trials of disease stages in COVID-19: complicated and often misinterpreted. *Lancet Glob Health*. 2020;8(10):e1249–e1250. doi:10.1016/S2214-109X(20)30365-X.
5. Dousa KM, Malavade SS, Furin J, et al. SARS-CoV-2 infection in a patient on chronic hydroxychloroquine therapy: implications for prophylaxis. *IDCases*. 2020;20:e00778. doi:10.1016/j.idcr.2020.e00778.
6. Schlagenhauf P, Hatz C, Behrens R, et al. Mefloquine at the crossroads? Implications for malaria chemoprophylaxis in Europe. *Travel Med Infect Dis*. 2015;13:192–196. doi:10.1016/j.tmaid.2015.03.010.
7. Fan HH, Wang LQ, Liu WL, et al. Repurposing of clinically approved drugs for treatment of coronavirus disease 2019 in a 2019-novel coronavirus (2019-nCoV) related coronavirus model. *Chin Med J (Engl)*. 2020;133(9):1051–1056. doi:10.1097/CM9.0000000000000797.
8. Casadevall A, Pirofski LA. The convalescent sera option for containing COVID-19. *J Clin Invest*. 2020;130:1545–1548. doi:10.1172/JCI138003.
9. Li L, Zhang W, Hu Y, et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19. A randomized clinical trial. *JAMA*. 2020;324(5):460. doi:10.1001/jama.2020.10044.
10. Liu M, Chen Z, Dai M-Y, et al. Lessons learned from early compassionate use of convalescent plasma on critically ill patients with COVID-19. *Transfusion*. 2020:1–7. doi:10.1111/trf.15975.
11. Liu L, Wang P, Nair MS, et al. Potent neutralizing antibodies directed to multiple epitopes on SARS-CoV-2 spike. *Nature*. 2020;584(7821):450–456. doi:10.1038/s41586-020-2571-7.
12. Ledford H. Antibody therapies could be a bridge to a coronavirus vaccine - but will the world benefit? *Nature*. 2020;584(7821):333–334. doi:10.1038/d41586-020-02360-y.