Is Hydroxychloroquine a Safe and Effective Choice for Covid-19 Prophylaxis

1Rodrigo Moisés de Almeida-Leite, 2Tais Rondello Bonatti, 3Carolina Rodrigues Ponzoni, 4Ana Cristina da Cunha Korndorfer and 5Solange Bifani Tavares da Silva

1Department of Medicine, Faculdade de Medicina de Jundiaí, Brazil  
2Department of Parasitic Diseases, Universidade Paulista, Brazil  
3Department of Intensive Care Medicine, Unimed Itatiba, Brazil  
4Department of Internal Medicine, Faculdade de Medicina de Teresópolis, Brazil  
5Department of Pediatrics, Faculdade de Medicina de Jundiaí, Brazil

Abstract: The authors speculate about the possibility of Hydroxychloroquine as Covid-19 Phrophylaxis in the dose of 400 mg per week. The authors compared the experience of Malaria prophylaxis in this dose, with acceptable safety profile. Also, we compared in vitro susceptibility of SARS-Cov-2 with that of Plasmodium falciparum. This agent show significant higher potency for the first. Also, the extended Half-life (40-50 days) make it an acceptable choice for prophylaxis. We also cite Brazilian experience with Chloroquinated Salt in the 1950s, its efficacy and feasibility. Lastly, we suggest that clinical trials should be conducted test this hypothesis.

Keywords: COVID-19, Pre-exposure Prophylaxis, Hydroxychloroquine

Hydroxychloroquine has been used for more than sixty-five years in diverse clinical settings around the globe. Current FDA approved uses are for Systemic Lupus Sclerosis, Discoid Lupus and treatment and prevention of malaria. The recommended dose for Malaria prophylaxis is 400 mg per week (Shippey et al., 2018).

Many agents have shown in vitro and pre-clinical activity against this virus, including Remdesivir, Chloroquine and Hydroxychloroquine (Wang et al., 2020). The latter has shown more potent antiviral activity against SARS-CoV-2 and a better safety profile when compared with chloroquine. Shippey et al. (2018; Wang et al., 2020) hydroxychloroquine half-maximal Effective Concentration (EC50) for SARS-CoV-2 is substantially lower when compared to that of chloroquine - hydroxychloroquine EC50 = 6.14 μM and chloroquine: EC50 = 23.90 μM. Sanders et al. (2020) also, Hydroxychloroquine has show more potent activity against SARS-CoV-2 when compared with activity against susceptible Plasmodium falciparum, expressed by a substantially lower minimum inhibitory concentration (Lim et al., 2009). Additionally, extended half-life of the drug, around 40-50 days 1, promote it as a reasonable alternative for Covid-19 prophylaxis, with better safety-profile and greater potency when compared to chloroquine (Sanders et al., 2020; Lim et al., 2009; Yao et al., 2020; Watson et al., 2018).

Notwithstanding promising pre-clinical evidence, caution should be taken before drawing conclusions about mass-strategy use. The exact mechanism by which Hydroxychloroquine inhibits SARS-CoV-2 in humans is yet unknown and may be different from that of Plasmodium spy (Sanders et al., 2020). For the latter, is accepted to be by acidification of lysosomes, whereas for SARS-CoV-2 is believed to be by endocytosis and membrane fusion prevention, coupled with host immunomodulatory effects (Sanders et al., 2020). This different pharmacodynamics may have implications in the efficacy as a prophylactic and therapeutic drug. Moreover, dose strategies are still obscure. To this date, is proposed that a lower dose of Hydroxychloroquine is adequate for Covid-19 when compared to Malaria. Whether this translates to prophylactic strategy is still unknown (Sanders et al., 2020).

Mass-prophylaxis with chloroquine or hydroxychloroquine has been considered as strategy for Covid-19 mitigation (Spinelli et al., 2020). Specifically in Brazil, Malaria mass prophylaxis with Pinotti Salt (chloroquinated salt) was conducted and found to be feasible and effective in the Amazon region during the 1950s and 1960s (Da Silva and Hochman, 2011).
To this date, limited evidence is available regarding in vivo efficacy in the treatment and prophylaxis of Covid-19. The scarce literature comprises mostly of retrospective analysis with demographically distinct groups. One ecological study conducted in France compared mortality time to double among 16 countries with mass use of chloroquine and hydroxychloroquine and compared to demographically similar countries without this strategy. This study show an statistically significant reduction in the $R^2$ from 0.97 to 0.73 with the mass-strategy use of anti-malarial drugs (Izoulet, 2020).

Additionally, the use of Hydroxychloroquine does not appear to significantly increase adverse effects, as noted by a recent retrospective analysis. These authors present the outcomes of early hydroxychloroquine associated with Azithromycin in the treatment of the new coronavirus disease. Overall mortality was reported to be 0.7% and the authors did not find increased likelihood of serious adverse effects (Million et al., 2020).

In light of the seriousness of the ongoing Covid-19 pandemic, effective mitigations strategies are desperately needed. To date, there is scant pre-clinical and limited in-vivo evidence for the efficacy of antimalarial drugs for Covid-19 phrophylaxis, with Hydroxychloroquine being a preferable choice for greater potency and better safety profile. Although many questions are still to be answered before broad use for these drugs with this purpose, including precise pharmacodynamics and effective dose, current evidence supports the promotion of clinical trials, which may pave way to a new use for this decade-old drug.

**Author’s Contributions**

All authors equally contributed in this work.

**Ethics**

The authors do not have any conflict of interests to declare. All authors have been personally and actively involved in substantive work leading to the manuscript and will hold themselves jointly and individually responsible for its content.

**References**


