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Opinion

# Hydroxychloroquine as a Therapeutic Option in COVID-19 Affected Patients. Is it a Good Therapeutic Option?

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A novel coronavirus disease (COVID-19), caused by infection with SARS-CoV-2, has swept across 31 provinces in China and over. Up today (May, 02, 2020), the coronavirus COVID-19 is affecting 209 countries, with 3413169 infected patients and more than 230000 deaths reported [1].

Due to the lack of effective antiviral therapy against COVID-19, current treatments are focused on symptomatic treatment. Fortunately, clinical trials are currently underway to validate one or more candidate specific drugs. Their design (Randomized, controlled trials, international multicentric, adaptive) gives hope for a validated treatment as soon as possible.

Chloroquine and its hydroxychloroquine metabolite are malaria drugs with virucidal activity *in vitro* (on SARS-Cov and SARS-Cov2) [2,3]. It does not act directly on the virus, but on the cells infected by the virus, by decreasing their infectious capacities. In fact, it is recently reported that Hydroxychloroquine use in patients suffering from COVID-19 affection, seems to be effective in limiting the replication of SARS-CoV-2 (virus causing COVID-19) *in vitro* and *in vivo* according some limited data recently published [2,3]. In one Open-Label Non-Randomized Clinical Trial [3], Gautret., *et al.* have shown that the use of 600 mg of hydroxychloroquine daily in twenty patients, leads to a significant reduction of the viral carriage at D6-post inclusion compared to controls. In the same study, it was established that the association of Azithromycin to hydroxychloroquine was significantly more efficient for virus elimination.

In one systematic review including Twenty three trials published in PubMed and EMBASE databases, from inception to 1-March-2020, Cortegiani., *et al.* [2] found that the use of Hydroxychloroquine is associated with the attenuation of the severe progression of COVID-19, with a significant reduction of the viral carriage.

Hydroxychloroquine might have many effects against a virus, such as, for example, disrupting the virus's ability to enter a cell. In fact, it could also have a negative effect on the link between the virus and its receptor on the cells to be infected. Moreover, Hydroxychloroquine may affect the cells infected by the virus, by decreasing their infectious capacities. Finally, hydroxychloroquine prescription leads to attenuate the severe progression of COVID-19 with inhibition of cytokine storm (TNF α and IL6) by suppressing T cell activation. Figure 1 shows the mechanisms of action of Hydroxychloroquine on COVID19. However, undesirable effects of chloroquine are numerous, hence the distrust of certain doctors and scientists regarding its massive delivery to patients with Covid-19. In fact, in addition to gastro-intestinal manifestations (nausea, vomiting...), the use of this therapy can be associated with the possibility of QT prolongation and arrhythmogenic death [2,3]. These results were not confirmed in a recent published study [4] including a largest reported cohort of COVID-19 patients including 201 patients treated for COVID-19 with chloroquine/hydroxychloroquine. In this study, 10 patients (5.0%) received chloroquine, 191 (95.0%) received hydroxychloroquine and 119 (59.2%) also received azithromycin. There are no occurrences

of Torsade de pointes (TdP) or arrhythmogenic death, reported in this study. Although use of these Drugs lead to QT prolongation, clinicians hardly ever needed to suspend this therapy. Further study of the need for QT interval monitoring is needed before final recommendations can be made.

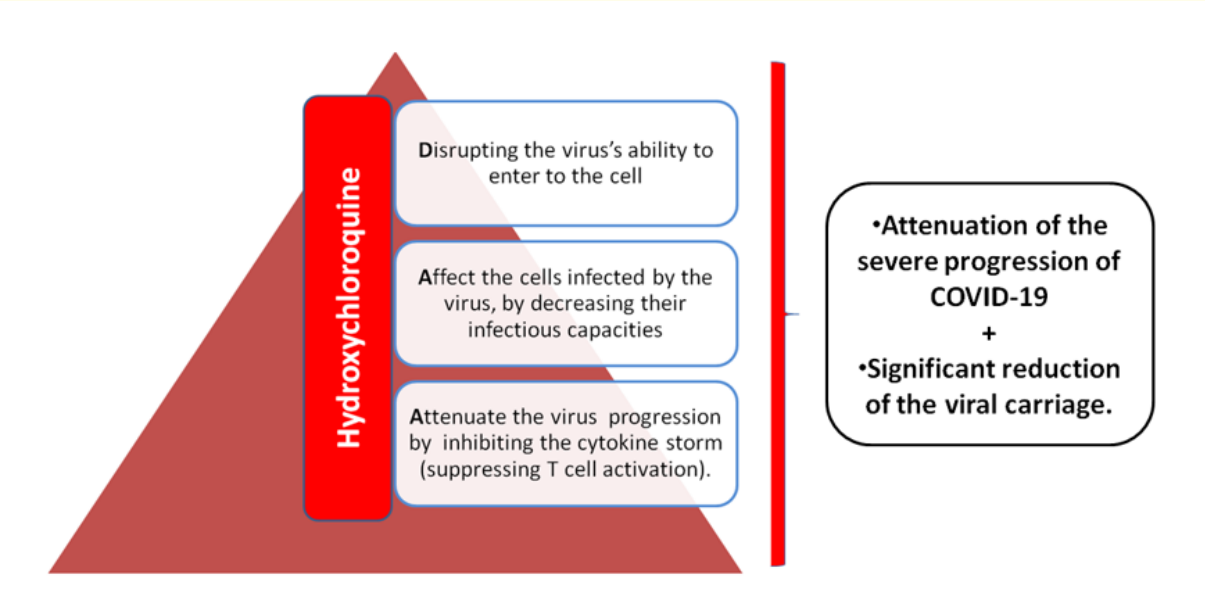


***Figure 1:*** *Mechanisms of action of Hydroxychloroquine on COVID19.*

More recently, the analysis of the use of hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19 in a big study including 96 032 patients (mean age 53.8 years, 46.3% women) with COVID-19 [5], didn't confirm the above results. In fact, when compared with mortality in the control group (9·3%), hydroxychloroquine, hydroxychloroquine with a macrolide, chloroquine, and chloroquine with a macrolide were each independently associated with an increased risk of in-hospital mortality. Moreover, the uses of these drugs were independently associated with an increased risk of de-novo ventricular arrhythmia during hospitalisation. For these reason, the World Health Organization has recommended a temporary suspension of clinical trials with hydroxychloroquine with partners in several countries.

In summary, although pre-clinical evidence of safety from long-time clinical use for other indications (such as, lupus erythematosus, Rheumatoid Arthritis…) was well established and that adaptive preliminary trials of chloroquine use in the treatment of COVID-19 have been encouraging, these results are not confirmed by a large multinational real-world analysis [5]. In the last study, the use of chloroquine or hydroxychloroquine was associated with an increased hazard for clinically significant occurrence of ventricular arrhythmias and increased risk of in-hospital death with COVID-19. For these reason, the World Health Organization has recommended the suspension of clinical trials with hydroxychloroquine with partners in several countries. For these reasons we cannot recommend the use of Hydroxychloroquine in patients suffering from COVID-19 affection.

## Authors' Contributions

All authors contributed to draft the manuscript. All authors read and approved the final manuscript.

## Competing Interests

The authors declare that they have no competing interests.

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