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Chloroquine and Hydroxychloroquine for Treatment of COVID-19

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In the face of the catastrophic outcomes of COVID-19 pandemic in several countries, scientists, physicians and politicians are eager for an effective treatment to save human lives, as well as to overcome the horrendous sanitary crisis and economic burden. Miraculous magic pills use to come out during chaotic sanitary problems like COVID-19 pandemic. That seems the case for the anti-malarial drugs chloroquine and its less toxic derivative hydroxychloroquine, which have been endorsed by some scientists, physicians and politicians as a magic cure for COVID-19 in several countries, based not in strong scientific evidence, but rather in preliminary and poor-quality reports. Miraculous and politically-motivated treatments without proper scientific evidence cause false hope to the patients and pose considerable risk to the population health. It follows that sounds extremely important to perform a comprehensive survey of the scientific literature on the use of chloroquine and hydroxychloroquine for COVID-19. In this paper, we revise the scientific literature in favour or against the use of chloroquine and hydroxychloroquine treatment for COVID-19. We conclude that these 4-aminoquinolines show some promising results in vitro, but not in preclinical studies in vivo, lacking clinical efficacy in trials performed so far in COVID-19 patients. Following transcription, translation of structural and non-structural viral proteins occurs in the ribosomes of host cells, following proteolytic processing by specific viral proteases, including chymotrypsin-like and papain-like proteases. After viral assembly, new viruses are released by exocytosis from the infected cell to spread infection to other cells in different organs. These steps of the virus cycle are putative targets for repurposing drugs. Chloroquine is a 4-aminoquinoline synthesized in 1934 by Hans Andersag working at Bayer laboratory. The drug was produced as a substitute to quinine – a pioneer and more toxic anti-malarial drug. Chloroquine toxicity was also decreased by adding an OH group to the N-ethyl at the end of the molecule, which produced a very similar, by less toxic 4-aminoquinoline named hydroxychloroquine (HC) in 1950s. Since then, both molecules have been used as anti-malarial drugs in several countries. The anti-malarial effect of HC is based on its action on the digestive vacuole of plasmodium, interfering with pH-dependent detoxification of heme radical, which is essential for protein synthesis in the parasite during hemoglobin consumption. It has been proposed that chloroquine and HC have anti-viral effects by increasing lysosomal pH and blocking autophagosome-lysosome fusion in vitro, interfering with endocytosis, which is pivotal for viral entry into the cell even in the presence of ACE-2. The rational for anti-viral effects of chloroquine and HC comes from in vitro studies of some viral diseases, while the pre-clinical studies using animal models presented conflicting or negative results. Chloroquine was effective *in vitro* against Ebola virus, but not in vivo Guinea pig model. For Chikungunya virus, anti-viral effects were reported in vitro, but exacerbating damage in animal models and lack of efficacy in clinical studies. The use of non-scientifically supported protocols for COVID-19, as already occurs in countries like Brazil and India, raises a false hope and poses a tremendous risk for the health of the people of those countries. Efficacious treatments for human diseases, including COVID-19, are matter of science not of faith or a political issue.

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