Chloroquine and Hydroxychloroquine Fact Sheet

Chloroquine was first used as an antimalarial drug over seventy years ago. Malaria is a disease of the blood caused by a parasite spread by the bite of infected mosquitos; malaria and the parasite that causes it are very different from the SARS-CoV-2 virus and the disease it causes, COVID-19. Chloroquine is taken by mouth and was very effective in the worldwide fight against malaria for many years before resistance decreased its antimalarial utility. Chloroquine was also found to be useful in treating other diseases, including lupus erythematosus. Hydroxychloroquine (brand name: Plaquenil) is closely related to chloroquine in terms of its chemical structure as shown below. In addition to being used to treat and prevent malaria in areas where parasites are not resistant to chloroquine, hydroxychloroquine is also used to treat lupus erythematosus and rheumatoid arthritis. The latter two conditions are not caused by infection.

Since chloroquine and hydroxychloroquine have been used clinically for many years, much is known about their safety. While these drugs cause a range of side effects, retinopathy is among the most common. For both chloroquine and hydroxychloroquine, retinopathy is most often associated with high or prolonged doses of these drugs. Cardiovascular side effects may be a concern in some cases, particularly if chloroquine or hydroxychloroquine are taken together with other drugs that may cause a similar side effect, such as azithromycin (see below).

Chloroquine and hydroxychloroquine affect the replication of several types of viruses in laboratory experiments [1, 2]. These related drugs make certain host cell compartments less acidic. Some viruses use these acidic compartments as they multiply within host cells. Thus, this loss of acidity caused by chloroquine and hydroxychloroquine can stop the replication of these viruses. Other mechanisms may also contribute to their antiviral effects. Recently, chloroquine and hydroxychloroquine have been used to treat COVID-19 associated pneumonia in China [3], and hydroxychloroquine was used in a small clinical study in France in people infected with COVID-19 [4]. Data from the studies performed in China have not yet been made available. In the French study, eight out of fourteen patients receiving hydroxychloroquine tested as negative for the virus six days after starting treatment, compared to 2/16 control patients testing as negative for COVID-19 six days after treatment began. When hydroxychloroquine was combined with azithromycin, an antibacterial drug, 6/6 patients receiving the combination were negative for the virus on day six after starting treatment. However, the study was performed with a small number of patients (only 36 patients in total), and six patients originally enrolled in the hydroxychloroquine treatment group were not included in the final analysis (lost in follow-up) for various reasons, including one death. The paper also reported whether the patients were positive or negative for the virus on day 6 and did not consider clinical outcome. It is also important to mention that this was an interim result; the study was still in process when the paper was published. Studies must be conducted in larger human trials to know whether chloroquine, hydroxychloroquine, and/or azithromycin are useful against COVID-19. According to clinicaltrials.gov, clinical studies to examine the efficacy
of hydroxychloroquine against COVID-19 are currently planned at Columbia University in New York and at the University of Minnesota. In the meantime, the recent death in an individual who ingested chloroquine present in a product intended for another purpose (treating pet fish, not disease in humans) highlights the dangers of self-medicating [5]. Indeed, the use of any drug outside the direction of a medical professional is likely to do more harm than good, advice highlighted in the FDA’s recent letter in response to this unfortunate death [6].

References


Updates

Posted on 4/13/2020: Since the use of chloroquine and hydroxychloroquine for COVID-19 is an evolving issue, we intend to provide periodic updates to this info piece by providing links to relevant articles and news reports.

Clinical study from Wuhan, Hubei Province, China of hydroxychloroquine in the treatment of COVID-19 patients with pneumonia (not peer-reviewed): https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2

Pilot study from Shanghai, China on hydroxychloroquine for the treatment of COVID-19 patients (abstract in English): DOI: 10.3785/j.issn.1008-9292.2020.03.03

Peer-reviewed study from Paris, France showing no evidence of clinical benefit from the hydroxychloroquine/azithromycin combination in patients with severe COVID-19 infections (available online 3/30/2020): doi.org/10.1016/j.medmal.2020.03.006

News article from the British Medical Journal concerning the US FDA’s authorization of the use of chloroquine and hydroxychloroquine for COVID-19 patients (dated 4/1/2020): https://www.bmj.com/content/369/bmj.m1335.long


Clinical study from Manaus, Brazil into the use of two different doses of chloroquine in hospitalized patients with COVID-19 indicating that the higher dose was not safe for patients (not peer-reviewed): https://www.medrxiv.org/content/10.1101/2020.04.07.20056424v1

**Posted on 5/28/2020:**


Study from Wuhan, Hubei Province, China indicating decreased mortality in patients critically ill with COVID-19 receiving hydroxychloroquine (not peer reviewed): https://www.medrxiv.org/content/10.1101/2020.04.27.20073379v1

Study from Madrid, Spain indicating that early hydroxychloroquine use leads to lower mortality in patients with mild COVID-19 symptoms upon hospital admission (not peer reviewed): DOI:10.20944/preprints202005.0057.v1

Peer reviewed article from the New England Journal of Medicine describing a study of COVID-19 patients receiving hydroxychloroquine conducted at New York–Presbyterian Hospital–Columbia University Irving Medical Center showing that hydroxychloroquine use led to neither an increased or decreased risk of death or intubation (dated 5/7/2020): DOI: 10.1056/NEJMoaa2012410


Multinational peer reviewed study of over 96,000 COVID-19 patients showing increased mortality and arrhythmia in those receiving hydroxychloroquine, chloroquine, and in those
receiving either of these drugs plus a macrolide (dated 5/22/2020) DOI: 10.1016/S0140-6736(20)31180-6.

Announcement by the World Health Organization that they have temporarily paused the arm of their Solidarity clinical trial involving hydroxychloroquine (dated 5/25/2020):

Recommendation by a French public health advisory against the use of hydroxychloroquine (with or without a macrolide) for COVID-19 (dated 5/26/2020):