Hydroxychloroquine/chloroquine

“To date, no acute virus infection has been successfully treated by chloroquine in humans.” [1]

Many different viruses can be inhibited in cell culture by both chloroquine and hydroxychloroquine, including the SARS coronavirus and ebolavirus. Some evidence for activity in animal studies has been found for a variety of viruses, including human coronavirus OC43, enterovirus EV-A71, Zika virus, and influenza A H5N1, and chikungunya virus. However, chloroquine has proven ineffective against influenza and dengue in human trials, and ebolavirus in mice in vivo. Chikungunya virus alphavirus replication in various animal models was enhanced by chloroquine. In human Chikungunya infection, chloroquine was ineffective and was associated with chronic arthralgias. [1]

From the online textbook UpToDate: “There are insufficient data thus far to know whether hydroxychloroquine or chloroquine has a role in the treatment of COVID-19. For this reason, we strongly recommend that patients should be referred to a clinical trial whenever possible. When a clinical trial is not available, we suggest not routinely using hydroxychloroquine or chloroquine, given the lack of clear benefit from limited data and potential for toxicity”. [2]

The margin between the therapeutic and toxic dose is narrow, and chloroquine poisoning has caused cardiovascular disorders that can be life-threatening. The most severe adverse effect when administering hydroxychloroquine or chloroquine for a short time is to prolong the QT interval on an EKG. In a patient with a prolonged baseline QTc interval or on other medications that prolong the QTc interval, this could result in cardiac arrhythmias.

Two unpublished randomized trials of hospitalized patients with mild to moderate COVID-19 compared standard of care to standard of care with hydroxychloroquine. [3] [4] Only one claimed to demonstrate any benefit, and this was rather far-fetched. Overall the study did not show any statistically significant benefit in clinical outcomes or clearing of the virus. The authors then went on to do 28 subgroup analyses, of which only one barely showed any statistically significant benefit. The authors were only able to claim any benefit of the treatment by manipulating statistical analyses and hiding data. [4]

A third unpublished trial comparing high and low dose chloroquine for COVID-19 was stopped early because high dose chloroquine caused more QTc prolongation and a trend toward higher lethality. The authors concluded that the higher CQ dosage should not be recommended for critically ill patients with COVID-19 because of its potential safety hazards, especially when

taken concurrently with azithromycin and oseltamivir, both of which prolong the QTc interval. [5]

In a randomized trial of 30 adults with COVID-19, the proportion of patients with nasopharyngeal viral clearance at day 7 in patients receiving hydroxychloroquine was the same as those receiving only standard of care. In addition, treatment with hydroxychloroquine did not improve clinical outcomes, and one patient in the hydroxychloroquine group progressed to severe disease. [6]

In contrast, the clearance rate of SARS-CoV-2 RNA on nasopharyngeal specimens was demonstrated to be enhanced in an open-label study of 36 adults with COVID-19. This is my favorite paper - “a real winner” - and yes, I do mean that sarcastically. In their discussion of the results, the authors are cautious to avoid any mention of clinical outcomes. A total of 26 patients received hydroxychloroquine, and 16 were control patients. Six hydroxychloroquine-treated patients were lost in follow-up during the survey because of early cessation of treatment. Reasons hydroxychloroquine-treated patients were removed from the trial: three patients were transferred to the intensive care unit; one patient died on day 3 post inclusion and was PCR-negative on day 2; one patient stopped the treatment on day three post-inclusion because of nausea. The sixth patient dropped out and went home. None of the control patients were lost to followup. The authors go on to conclude, “We therefore recommend that COVID-19 patients be treated with hydroxychloroquine and azithromycin to cure their infection and to limit the transmission of the virus to other people to curb the spread of COVID-19 in the world.” [7], Interestingly, the one reported death is associated with clearing of the virus. It seems to me that a more fitting conclusion would be “clear the virus, kill the patient,” or “win the battle, lose the war.”

In a small study of 7 men and 4 women with a mean age of 58.7 years, Molina et al., using the same dosing regimen reported by Gautret et al., published their results in a letter entitled "No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection". [8] Res ipsa loquitur.

Most recently, a paper posted on April 14, 2020, was titled “No evidence of clinical efficacy of hydroxychloroquine in patients hospitalized for COVID-19 infection with oxygen requirement”. [9] Again, the title speaks for itself.

Vitamin C, anyone? Got glutathione? A little zinc with that? I'll pass on the hydroxychloroquine.

Disclaimer: As always, talk to your doctor or the President of the United States before making any health-related decisions.

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