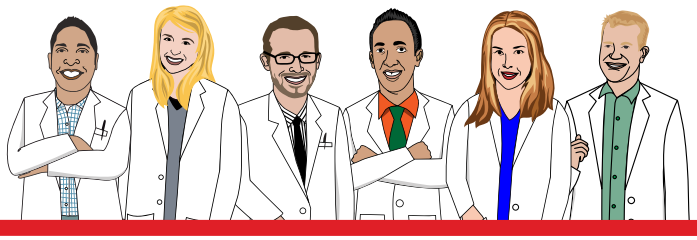
Emergency Medical Abstracts



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A randomized trial of hydroxychloroquine as postexposure prophylaxis for Covid-19

Boulware DR, Pullen MF, Bangdiwala AS, et al. N Engl J Med. 2020;383(6):517-525.

SUMMARY:

- The antimalarial agent hydroxychloroquine (as well as chloroquine) has in vitro activity against SARS-CoV and SARS-CoV-2 (which causes COVID-19). Hydroxychloroquine interferes with angiotensin-converting enzyme 2 at the point of SARS CoV-2 binding, thus potentially affecting the ability of the virus to enter cells. Hydroxychloroquine has been shown to be ineffective in symptomatic people. There is no high-quality evidence suggesting that hydroxychloroquine decreases mortality or hospitalization. Some have argued that this lack of evidence is because hydroxychloroquine should be used to prevent but not treat infection.
- This study asked whether hydroxychloroquine might prevent new SARS-CoV-2 infection among people experiencing high- or moderate-risk exposure (postexposure prophylaxis).
- Adult patients were required to have been exposed to someone with confirmed COVID-19 (household or occupational exposure) and to not have used a mask or practiced social distancing from that person for more than 3 days before enrollment. The study enrolled participants at multiple sites throughout the U.S. and Canada. Participants self-enrolled by replying to social-media outreach and indicating that they had been exposed. A research pharmacist mailed eligible participants either hydroxychloroquine or placebo. (The hydroxychloroquine dose was 600 mg daily for 4 days, with a loading dose of 1,400 mg on day 1.)
- The primary outcome was the development of confirmed COVID-19 or COVID-like illness within 14 days, as reported by the patients, who filled out a symptom checklist every few days for up to 6 weeks. The secondary outcomes included hospitalization and death.
- The authors initially intended to enroll 1,500 people but ultimately stopped after 821, partly because the infection rate was higher than estimated in the original power calculation, and therefore the power of those 821 participants was higher than expected. The authors actually enrolled 921 participants, but 100 developed symptoms on day 1 and were excluded a priori. The mean patient age was 40 years, and two-thirds were health care workers. Most had exposure 3 or 4 days before they began taking the pills.
- Ultimately, 13% of the participants developed COVID-19: 11.8% in the hydroxychloroquine group vs 14.3% in the placebo group (P = .35). A total of 2 hospitalizations, no deaths, and no arrhythmias occurred.
- Of those who took hydroxychloroquine, 40% reported an adverse affect, as compared with 16.8% of those who took the placebo. The adverse affects were always considered mild and self-limited.
- This study has many limitations, including that participant identification was self-reported, as was the primary outcome of interest. In addition, medication adherence was not assessed, the study was powered to detect only a 50% treatment effect, and patients had been exposed for 3-4 days before they began taking the study drug.

PMID: 32492293

FULL ARTICLE: https://www.nejm.org/doi/10.1056/NEJMoa2016638?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

EDITOR'S COMMENTARY: **This is a large RCT of hydroxychloroquine vs placebo for the prevention of COVID-19 after risky exposure. The rate of infection was approximately 13% and did not vary significantly between those who received hydroxychloroquine and those who did not. Proponents will point to the study's limitations to argue that hydroxychloroquine may have value if administered earlier or in select cases. This argument could be true, but there is no evidence supporting it. To date, no high-quality data have demonstrated that hydroxychloroquine is effective in postexposure prophylaxis.**

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