Hydroxychloroquine for the Prevention of Covid-19

Searching for Evidence

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus that causes coronavirus disease 2019 (COVID-19). The infection of the spread of this pandemic. The introduction of the spread

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intended to provide an intervention in the shortest possible time to prevent infection. In a small-animal model of SARS-CoV-2 infection,\(^8\) prevention of infection or more severe disease was observed only when the experimental antiviral agent was given before or shortly after exposure. In the current trial, the long delay between perceived exposure to SARS-CoV-2 and the initiation of hydroxychloroquine (23 days in most participants) suggests that what was being assessed was prevention of symptoms or progression of Covid-19, rather than prevention of SARS-CoV-2 infection.

Drugs for the prevention of infections must have an excellent safety profile. When hydroxychloroquine was initially promoted as a possible solution to SARS-CoV-2 infection, the safety of the drug was emphasized.\(^2\) Under closer scrutiny, however, the potential for cardiac toxic effects and overall adverse outcomes have been emphasized, especially in persons with underlying coexisting conditions that increase the risk of severe Covid-19.\(^9\) Boulware et al. report frequent mild side effects of hydroxychloroquine, but cardiac toxic effects could not be assessed.

So, what are we to do with the results of this trial? The advocacy and widespread use of hydroxychloroquine seem to reflect a reasonable fear of SARS-CoV-2 infection. However, it would appear that to some extent the media and social forces — rather than medical evidence — are driving clinical decisions and the global Covid-19 research agenda.\(^10\) On June 1, 2020, ClinicalTrials.gov listed a remarkable 203 Covid-19 trials with hydroxychloroquine, 60 of which were focused on prophylaxis. An important question is to what extent the article by Boulware et al. should affect planned or ongoing hydroxychloroquine trials. If postexposure prophylaxis with hydroxychloroquine does not prevent symptomatic SARS-CoV-2 infection (with recognition of the limitations of the trial under discussion), should other trials of postexposure prophylaxis with hydroxychloroquine continue unchanged? Do the participants in these trials need to be informed of these results? Do these trial results with respect to postexposure prophylaxis affect trials of preexposure prophylaxis with hydroxychloroquine, some of which are very large (e.g., the Healthcare Worker Exposure Response and Outcomes of Hydroxychloroquine [HERO-HCQ] trial, involving 15,000 health care workers; ClinicalTrials.gov number, NCT04334148)? The results reported by Boulware et al. are more provocative than definitive, suggesting that the potential prevention benefits of hydroxychloroquine remain to be determined.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.