UPDATE ALERTS

Update Alert: Hydroxychloroquine or Chloroquine for the Treatment or Prophylaxis of COVID-19

This report updates our living systematic review assessing hydroxychloroquine or chloroquine versus control therapy for the treatment of coronavirus disease 2019 (COVID-19) in hospitalized patients, which covered evidence available through 8 May 2020 (1). Using the same methods, we searched for and evaluated evidence published through 1 July 2020.

Additional Eligible Evidence Identified

Published reports of 3 studies previously available as preprints became available (2–4), enabling more thorough assessment for risk of bias. The risk of bias is now determined to be serious for Yu and colleagues' study (4), remains high for Tang and colleagues' study (2), and changed from moderate to serious for Mahévas and colleagues' study (3). We found 1 new randomized controlled trial (RCT) with high risk of bias (5), 1 new cohort study with moderate risk of bias (6), and 4 cohort studies that each had serious risk of bias (7–10). An additional large cohort study was published and subsequently retracted due to concerns about the veracity of the data (11, 12) and was not considered further. Press releases reported 3 large RCTs (RECOVERY, SOLIDARITY-WHO, and ORCHID-NIH) that ceased enrollment for the hydroxychloroquine versus control comparison early because of lack of efficacy in preliminary analyses (13–15). These trials had strong study designs, but other than press releases, no reports were available to assess.

The only new data on chloroquine came from Chen and colleagues' aforementioned RCT, which contained a chloroquine group that was compared with a control group (5). This RCT had high risk of bias and observed no deaths or severe disease progression, and all patients in both groups cleared the virus from the upper respiratory tract by day 10 (5). However, clinical recovery took fewer days in the chloroquine group than the control group.

Updated Evidence Synthesis

Supplement Tables 1 and 2 (available at Annals.org) provide updated unadjusted outcomes data (1–28). Given the risk of bias for individual studies and the conflicting direction and magnitude of results, the evidence from both RCTs and cohort studies remains insufficiently strong to support a benefit of hydroxychloroquine or chloroquine for treatment of COVID-19 in hospitalized patients. We were unable to identify a pattern by which risk of bias, dosage, duration of therapy, or other factors explained the conflicting findings. The strength of evidence remains insufficient for all safety outcomes.

Discussion

This update identified 1 new RCT, several new cohort studies, and more complete published reports of studies previously available as preprints; the conclusions are unchanged from the initial review. The newly available evidence has high risk of bias. There is insufficient evidence to support the effectiveness or safety of hydroxychloroquine or chloroquine for the treatment of COVID-19 in hospitalized patients.

The results of the RECOVERY, SOLIDARITY-WHO, and ORCHID-NIH trials could help to more definitively determine the role of this therapy for COVID-19.

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