UAMS EM Journal Club
April 2020 JC Summary
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Morbidity and Mortality Effects on Hydroxychloroquine Use in COVID-10 Patients

Clinical Bottom Line

While many medications are being repurposed for use in the treatment of patients with COVID-19, their clinical significance is not well studied. Hydroxychloroquine specifically, which was very popular in the early stages of the pandemic as a possible therapy, was not found to have a mortality benefit and may also cause harmful side effects such as increased rates of cardiac arrest and EKG changes. Hydroxychloroquine should not routinely be used in the treatment of patients with COVID-19.

P:Patients with COVID -19
I: Hydroxychloroquine
C: Standard therapy
O: Mortality and Adverse events

Trial 1 (systematic review)

Chowdhury, et al. “A Rapid Systematic Review of Clinical Trials Utilizing Chloroquine and Hydroxychloroquine as a Treatment for COVID-19.” *Acad Emerg Med, accepted but not yet published.*

Full text link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7267507/

Validity Rating

High risk of bias. Low quality of evidence. Systematic review.

The Basics

Literature search was performed evaluating for studies involving hydroxychloroquine treatment in COVID-19 positive patients. Ultimately, only 7 studies could be included which were dissimilar in design with variable results, which significantly limited the assessment. Due to significant heterogeneity, no meta-analysis was able to be performed.

Inclusion Criteria for Review

1) Randomized or non-randomized clinical trials assessing the efficacy or safety of HCQ or CQ use in patients with COVID-19.
2) Participants in the trials could be of any age, in any geographical location.
3) Published articles, pre-print manuscripts, abstracts, letter to the editors’ or currently
4) Completed between December 1st, 2019 to April 26th, 2020.

Primary and Secondary Outcomes

Extremely variable within the studies. Common outcomes assessed included viral clearance based on PCR, resolution of symptoms (such as cough or fever), mortality, length of hospitalization.

Results

5 of the 7 studies showed favorable results with use of hydroxychloroquine, but had major flaws in study design, increased risk of bias and small sample sizes. 2/7 showed no benefit but were susceptible to similar problems. Overall the review was unable to directly combine the studies secondary to significant heterogeneity, so no meta-analysis was able to be performed.

Limitations and Bias

-heterogeneity of study design
-methodological flaws in multiple studies
-incomplete data
-underpowered in many cases
-utilizing Cochrane Risk Bias Tool 2.0, all studies had at least one area with high risk of bias, except for Chen, Zhaowei, et al. “Efficacy of Hydroxychloroquine in Patients with COVID-19: Results of a Randomized Clinical Trial .” (MedRxiv, www.medrxiv.org/content/10.1101/2020.03.22.20040758v3), however this study had concerning methodological flaws

Trial 2

Rosenberg ES, Dufort E, Udo T, et al. “Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State.” *The Journal of the American Medical Association. 2020 May*

https://jamanetwork.com/journals/jama/fullarticle/2766117

Validity Rating

Low risk of bias. Moderate quality of evidence. Retrospective cohort study.

The Basics

This retrospective cohort study looked at all patients with a confirmed diagnosis of COVID-19 in NYC and the association of hydroxychloroquine +/- Azithromycin use with in-hospital mortality. A random sample of patients (n=1438) out of all patients diagnosed with laboratory confirmed COVID-19 in NYC were included in the study. The electronic health record was used to track the pre-defined outcomes of interest. These outcomes were adjusted for demographics as well as illness severity and analyzed. They looked at patients receiving hydroxychloroquine + azithromycin compared to neither treatment, hydroxychloroquine alone compared to standard treatment, azithromycin alone compared to standard treatment, and hydroxychloroquine alone vs azithromycin alone.

Inclusion Criteria

- Presented during a 2 week pre-designated period in March (3/15-28) in a NYC hospital

- Admitted for at least 24 hours
- Have laboratory confirmed positive COVID-19.

Exclusion Criteria

- Admission period of less than 24 hours
- Chart being too incomplete for review

Primary Outcomes

In-Hospital Mortality

Secondary Outcomes

Cardiac arrest and EKG abnormalities

Results

- There were no significant differences in in-hospital mortality between the different groups when adjusted for confounding variables.
- Patients had higher odds of cardiac arrest if they were on Hydroxycholorquine and azithromycin compared to neither drug (OR 2.13; [95% CI, 1.12-4.05]) as well as hydroxychloroquine alone vs azithromycin alone (OR 2.97; [95% CI, 1.56-5.64]).
- There was no statistical difference between the treatment arms regarding odds of developing abnormal ECG findings.

Limitations and Bias

- Bias limited as measuring objective outcomes such as mortality, presence of cardiac arrest, and EKG changes
- Definition of EKG changes not well defined
- How they count cardiac arrest was not well defined
- Some patients were still admitted at the end of the study period