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The Use of Hydroxychloroquine for COVID-19

Introduction

1. SARS-CoV-2, also known as COVID-19, is a betacoronavirus and shares genetic sequence and viral structure with both severe acute respiratory syndrome coronavirus (SARS-CoV; 70% similarity) and Middle East respiratory syndrome coronavirus (MERS-CoV; 40% similarity).
2. COVID-19 has created a global health emergency with multiple phjpatkaarmacologic agents displaying activity in vitro.
3. Hydroxychloroquine (HCQ) and chloroquine (CQ) have been publicized by various sources leading to use to manage COVID-19.
4. There have been few well conducted clinical studies with patient-centered outcomes to guide therapy which makes this therapy controversial.

Pharmacology	
Hydroxychloroquine (Plaquenil)	
Dose	• 400 mg twice daily for 1 day followed by 200 mg twice daily ○ Studies report alternative dosing using 400-600 mg total daily dose Dose Adjustments • GFR <30 mL/min: Consider dose reduction of 50% • Liver dysfunction: Use caution in patients
Administration	• Do not crush or divide film-coated tablets ○ Some sources suggest that tablets can be compounded into an oral solution
Formulation	• 200 mg tablet
PK/PD	• Time to Peak Concentration: 2-3 hours • Metabolism: Extensively by liver • Elimination: Urine 15% to 25%
Adverse Effects	• QTc prolongation • Hypoglycemia • Neuropsychiatric effects • Retinopathy • Cardiotoxicity
Drug Interactions and warnings	• Additive QT-Interval prolongation when taking concomitant QT-interval prolonging medications such as azithromycin and fluoroquinolones
Comments	• Use of chloroquine and hydroxychloroquine in pregnancy is generally considered safe

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Author, year	Design/ sample size/ location	Intervention & Comparison	Outcome
Molina, 2020	Observational study in France n=11	• HCQ 600 mg daily x 10 days + azithromycin 500 mg day 1 then 250 mg day 2-5 • Conventional treatments without HCQ	• **No reduction in Nasopharyngeal PCR samples** at days 5 and 6 in **8/10 pts tested**
Wang, 2020	Multi-center, open-label RCT n=150	• HCQ 1,200 mg daily for three days, followed by 800 mg daily for 2-3 weeks • Conventional treatments without HCQ	• **No difference in viral clearance by 28 days between intervention and standard of care** • Adjusted analysis **found some improvement in symptoms with HCQ** compared to therapy without HCQ
Chen Z, 2020	RCT in China n=61	• HCQ 200 mg/bid x 5 days • Conventional treatments without HCQ	• Cough remission time, improved pneumonia, and temperature recovery time significantly **shortened in the HCQ treatment group** • Median duration from hospitalization to viral nucleic acid negative conservation and radiological progression on CT **no different between groups**
Gautret, 2020	Observational study in France n= 36	• HCQ 200 mg tid x 10 days • HCQ 200 mg 3 tid x 10 days + azithromycin 500 mg day 1 then 250 mg day 2-5 • Conventional treatments without HCQ	• At day 6, **more patients treated with HCQ (57%) and (100%) in patient treated with HCQ+ azithromycin had negative PCR results compared** to the control group
Chen J, 2020	RCT in China n=30	• HCQ 400 mg per day x 5 days + conventional treatments • Conventional treatments without HCQ	• **No difference** in negative PCR at day 7 in HCQ vs. control group (86.7% vs 93.3%) • **No difference between groups** for median duration from hospitalization to negative conversion and temperature normalization • **Excluded patients with severe and critical illness**

Conclusion

- **Current studies have had significant methodological flaws, are not peer-reviewed, and conducted in patients that were mild compared to the sicker patients that these therapies are applied to**. There are multiple randomized controlled trials currently being conducted and most societal guidelines recommend this therapy being used in a randomized controlled trial. Clinicians should weigh the controversial benefits and risks for each patient. Until more studies are released there is isn't a strong recommendation for or against the use of Hydroxychloroquine for the use of COVID-19.

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