Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19 (U.S.)

Source: Geleris J, et al. N Engl J Med. 2020 May 7. [Epub ahead of print]
Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19: Design

| Study Design |
|--------------|
| **Background**: Retrospective cohort study of 1446 consecutive, hospitalized patients at a New York City hospital from March 7 to April 8, 2020. |
| **Location**: New York City |
| **Inclusion Criteria (n = 1,446 evaluated; 1376 included in analysis)** |
| - Positive NP or OP swab for SARS-CoV-2 by PCR |
| - Admission to hospital |
| - Age ≥18 years |
| **Exclusion Criteria** |
| - Patients who died, were intubated, or transferred within 24 hours of admission |
| - 70 patients were excluded from analysis based on these criteria |
| **Primary Endpoint** |
| - Time to intubation or death. |
| **Duration of follow up** |
| - Through April 25, 2020 |

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| Study Design |
|--------------|
| **Hospital Treatment Guidance for Use of Hydroxychloroquine**  |
| - Therapeutic option: patients with COVID-19 with “moderate-to-severe” respiratory illness  |
| - Moderate-to-Severe Respiratory Illness: defined as SpO2 < 94% on ambient air  |
| **Hydroxychloroquine Dosing and Duration**  |
| - 600 mg twice daily on day 1, then 400 mg daily (median 5 days)  |
| - 85.9% received hydroxychloroquine <48 hours of presentation to emergency department  |
| **Suggested Additional Therapy (until April 12, 2020)**  |
| - Azithromycin: 500 mg day 1, then 250 mg daily for 4 additional days  |
| **Definition of Hydroxychloroquine Exposure**  |
| - Receiving hydroxychloroquine at baseline or prior to intubation or death  |
| **Statistical Analysis**  |
| - Propensity scoring was used to account for reduce the effect of confounding by indication  |
| - Propensity score included:  |
| - Demographic factors  |
| - Clinical factors  |
| - Laboratory tests  |
| - Medications  |

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Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19: Baseline Characteristics

| Baseline Characteristics* | Hydroxychloroquine (n = 811) | No hydroxychloroquine (n = 565) |
|---------------------------|------------------------------|---------------------------------|
| Age ≥60 years, n (%)      | 514 (63.4)                   | 318 (56.2)                      |
| Female, n (%)             | 337 (41.6)                   | 258 (45.7)                      |
| Coexisting conditions, n (%) |                              |                                 |
| Hypertension              | 398 (49.1)                   | 38 (6.7)                        |
| Diabetes                  | 301 (37.1)                   | 190 (33.6)                      |
| Chronic lung disease      | 146 (18.0)                   | 105 (18.6)                      |
| Oxygen saturation %, median (IQR) | 94 (90 – 96)               | 96 (94 – 98)                    |

*Unmatched patients differed in hydroxychloroquine exposure by: age, race and ethnic group, BMI, insurance, smoking status, and current use of other medications

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| Concomitant Therapy, n (%) | Hydroxychloroquine (n = 811) | No hydroxychloroquine (n = 565) |
|---------------------------|-------------------------------|---------------------------------|
| Statin                    | 308 (38.0)                    | 197 (34.9)                      |
| ACE Inhibitor or ARB      | 236 (29.1)                    | 142 (25.1)                      |
| Systemic glucocorticoid  | 216 (26.6%)                   | 57 (10.1)                       |
| Azithromycin              | 486 (59.9)                    | 127 (22.5)                      |
| Tocilizumab               | 58 (7.2)                      | 12 (2.1)                        |
| Remdesivir                | 22 (2.7)                      | 5 (0.9)                         |

Abbreviations: ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker

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Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19: Results

| Analysis                                           | Intubation or Death       |
|----------------------------------------------------|---------------------------|
| No of events/no of patients at risk (%)            |                           |
| Hydroxychloroquine                                 | 262/811 (32.3)            |
| No hydroxychloroquine                             | 84/565 (14.9)             |
| Crude analysis – HR (95% CI)                       | 2.37 (1.84 – 3.02)        |
| Adjusted for propensity score – HR (95% CI)        | 0.97 (0.74 – 1.28)        |

* Additional sensitivity analyses, including those that used a different baseline of 48hrs after admission and those that defined treatment as starting hydroxychloroquine prior to study admission showed similar results.

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Freedom from Composite End Point of Intubation or Death. The shaded areas represent pointwise 95% confidence intervals.

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• Total Enrollment for Analysis (n = 1376)
  - 811 (58.9%) received hydroxychloroquine
  - 565 (41.1%) did not receive hydroxychloroquine

• Timing of Receipt of Hydroxychloroquine
  - 45.8% received <24 hours of presentation to the emergency department
  - 85.9% received <48 hours of presentation to the emergency department

• Risk of Intubation or Death
  - Multivariable analysis showed no significant difference among patients who received hydroxychloroquine than among those who did not

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Conclusions: “In this observational study involving patients with Covid-19 who had been admitted to the hospital, hydroxychloroquine administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death. Randomized, controlled trials of hydroxychloroquine in patients with Covid-19 are needed.”