COVID-19 Rapid Reviews

Along with regular Tools for Practice, the PEER team will be writing rapid reviews to address COVID-19 topics relevant for primary care. The evidence is changing rapidly and it is possible that as you read this, new evidence will already be available. We will try our best to stay in front and keep you up-to-date during these challenging times.

Hydroxychloroquine with or without azithromycin for COVID-19

Clinical Question: Is hydroxychloroquine (with or without azithromycin) effective in treating COVID-19?

Bottom Line: One nonrandomized study found that more hydroxychloroquine/azithromycin patients tested negative for virus at days 3 and 6 but clinical outcomes were not reported. One unblinded randomized trial showed no effect from hydroxychloroquine on viral or clinical outcomes. Without further evidence, hydroxychloroquine is not appropriate for patients with COVID-19 in primary care.

Evidence:
- One non-blinded randomized study in China (30 in-patients, mean age 48).\(^1\)
  - Hydroxychloroquine 400 mg daily for 5 days was given to one group and both groups received conventional treatments.
    - Number with negative PCR nasopharyngeal swab:

<table>
<thead>
<tr>
<th></th>
<th>Day 7</th>
<th>Adverse effects (examples diarrhea and elevated aspartate aminotransferase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>14/15 (93%)</td>
<td>3/15</td>
</tr>
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Hydroxychloroquine | 13/15 (87%) | 4/15

- Median time to temperature normalization was 1 day in each group.
- All patients survived.
- Limitations: not blinded. Much of the text was in Chinese.

- One non-randomized study in France (42 in-patients, mean age 45) of hydroxychloroquine 200mg three times daily for 10 days. Antibiotics could be added to prevent bacterial superinfection based on clinical judgement (azithromycin 500mg for 1 day then 250mg daily for 4 days).
  - Number with negative PCR nasopharyngeal swab:

<table>
<thead>
<tr>
<th></th>
<th>Day 3</th>
<th>Day 6</th>
</tr>
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<tbody>
<tr>
<td>Control</td>
<td>1/16 (6%)</td>
<td>2/16 (13%)</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>5/14 (36%)</td>
<td>8/14 (57%)</td>
</tr>
<tr>
<td>Hydroxychloroquine + Azithromycin</td>
<td>5/6 (83%)</td>
<td>6/6 (100%)</td>
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</tbody>
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- Limitations: not randomized, no clinical outcomes or adverse effects reported, 6 hydroxychloroquine patients lost to follow-up and not analyzed (including 1 death and 3 transferred to critical care).

**Context:**
- There are no studies evaluating the use of hydroxychloroquine to prevent COVID-19 infection.
- At least 23 other clinical trials currently in progress.
- Both azithromycin and hydroxychloroquine are associated with an increased risk of sudden cardiac death from QT prolongation.
- Applying early data, when we really need treatments and hope, is challenging. However, interventions that have not been verified to provide clinical/symptomatic benefits for hospitalized patients with COVID-19 are unlikely to benefit patients in primary care.

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**Disclosures:**
Authors do not have any conflicts of interest to declare.

**References:**