A meta-review of meta-analyses and an updated meta-analysis on the efficacy of chloroquine and hydroxychloroquine in treating COVID19 infection

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Background
- Controversy surrounds the efficacy of the antimalarial drug chloroquine (CQ), and its derivative, hydroxychloroquine (HCQ), on their efficacy and possible harm when used for the treatment of COVID19.
- Findings from meta-analyses, and primary studies have produced conflicting findings on the efficacy and safety of these drugs.

Aims & Objectives
- To synthesize the findings from systematic reviews and meta-analyses as well as to update the evidence using a meta-analysis in evaluating the efficacy and safety of CQ and HCQ with or without Azithromycin for the treatment of COVID19 infection.

Methods
- A meta-review of published systematic reviews and updated meta-analysis of experimental studies where either HCQ or CQ with or without Azithromycin were used for the treatment of COVID19.

Search strategy:

<table>
<thead>
<tr>
<th>Databases</th>
<th>Keywords</th>
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<tbody>
<tr>
<td>CINAHL</td>
<td>&quot;COVID-19&quot;, &quot;hydroxychloroquine&quot;, &quot;chloroquine&quot;, &quot;Azithromycin&quot;</td>
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<tr>
<td>EMBASE</td>
<td>&quot;COVID-19&quot;, &quot;cloroquina&quot;, &quot;hidroxicloroquina&quot;, &quot;azitromicina&quot;</td>
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<td>MEDLINE</td>
<td>&quot;COVID-19&quot;, &quot;chloroquine&quot;, &quot;hydroxychloroquine&quot;, &quot;Azithromycin&quot;</td>
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<td>SCOPUS</td>
<td>&quot;COVID-19&quot;, &quot;chloroquine&quot;, &quot;hydroxychloroquine&quot;, &quot;Azithromycin&quot;</td>
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<tr>
<td>CRANIAL</td>
<td>&quot;COVID-19&quot;, &quot;hydroxychloroquine&quot;, &quot;chloroquine&quot;, &quot;Azithromycin&quot;</td>
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Data extraction:
- For each study, two authors independently extracted data and assessed quality.

Quality Assessment:
- Risk of bias was assessed using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool for reviews and the MethodologicAI Standard for Epidemiologic Research (MASTER) scale for the experimental studies.

Outcomes:
- The main outcome for both the meta-review and the updated meta-analysis was mortality. Secondary outcomes were transfer to the intensive care unit (ICU) or mechanical ventilation, worsening of illness, viral clearance and the occurrence of adverse events.

Synthesis of findings:
- Synthesis of findings from different reviews was done using a combination of a structured summary of findings from the reviews and presentation in forest plots.
- For the updated meta-analysis, findings from included experimental studies were synthesized using quality effect model.
- The Cochran Q test p-value was used to test for and the I² statistic to quantify heterogeneity.

Results

Meta-review of systematic reviews results

- All-cause of mortality
- Over all, all meta-analyses showed higher risk of mortality with HCQ with/without Azithromycin, compared to control (Fig 3).

Virological cure and adverse events

- Most meta-analyses found no significant differences between HCQ group and control, in virological cure but significantly higher risk of adverse events for HCQ (Fig 4).

Secondary outcomes

- No significant differences between the groups in the risks of ICU transfer/mechanical ventilation, virological cure, and disease exacerbation. There was a significantly higher risk of adverse events in participants who received HCQ compared to those on standard care (Fig 6).

Conclusion
- There is conclusive evidence that CQ and HCQ, with or without Azithromycin are not effective in treating COVID-19 or its exacerbation.

References