Chloroquine Phosphate is not Proved to be an Effective Treatment for Coronavirus: A Meta-analysis of Clinical Trials

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On 31 December 2019, the Chinese health authorities declared an outbreak of a novel coronavirus (COVID-19), which rapidly extended in many countries. On 11 March 2020, the World Health Organization (WHO), after reported outbreaks in more than 110 countries, declaring COVID-19 as a pandemic [1].

Currently, vaccines and antivirals for COVID-19 are being investigated around the world [2]. Several reports claimed that chloroquine phosphate (chloroquine) could be an effective treatment for patients with COVID-19, by inhibiting viral entry into the host cells [3].

The aim of this meta-analysis is to investigate the effectiveness of chloroquine in treating coronavirus, in general not only COVID-19, by pooling the results of Randomized Controlled Clinical Trials (RCTs).

A comprehensive PubMed search (from July 1966 until 15 March 2020) was conducted using a variety of Medical Subjects Headings and free text words: coronavirus and chloroquine and/or clinical trials. Additional searches were conducted in Cochrane Central Register of Controlled Trials, Trip Database, Science Direct, and previously published reviews. No attempts were made to locate any unpublished studies.

Only 28 publications were identified, none of which was a RCT. Identified studies were published between 1987 and 2020.

Of these 28 publications, 7 were published in 2020 and discussed the effectiveness of chloroquine against COVID-19 [4 - 10]:

[I] Multicenter clinical trials currently conducted in China with only promising results that chloroquine could be effective for treating COVID-19 (2 publications).

[II] Expert consensus on the usage of chloroquine for treating COVID-19 associated to pneumonia (1 publication).

[III] Reviews and recommendations in the light of old experiments (2 publications).

[IV] \textit{in vitro} experiments, with one comparing chloroquine with hydroxychloroquine (2 publications).

Table 1 summarizes the types of studies and the results of each.

Table 1. Summary of published studies in 2020 evaluating the effectiveness of chloroquine for treatment of COVID-19.

<table>
<thead>
<tr>
<th>References</th>
<th>Type of Study</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>Yao \textit{et al.} [5]</td>
<td>\textit{In vitro} Antiviral Activity of Hydroxychloroquine against Severe Acute Respiratory Syndrome COVID-19.</td>
<td>Hydroxychloroquine was found to be more potent than chloroquine to inhibit COVID-19.</td>
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Till 15 March 2020, the final results of the clinical trials currently conducted in China were not available, only the preliminary results reported promising effectiveness of chloroquine against COVID-19 [11].

The other 21 publications not related to COVID-19 were distributed as follows; in vitro experiments (11 publications), in vivo experiments (5 publications), both in vitro and in vivo experiments (1 publication), and reviews (4 publications). Only 2 in vitro experiments were about Middle East Respiratory Syndrome coronavirus (MERS-CoV) and 5 publications (2 in vitro experiments, 2 reviews, and 1 in vivo experiment) were about Severe Acute Respiratory Syndrome coronavirus (SARS-CoV).

CONCLUSION

In conclusion, this meta-analysis could not prove that chloroquine is an effective treatment against coronavirus in general or COVID-19 in particular. Expanded access trials should be encouraged especially stating that chloroquine is available, cheap and relatively safe drug.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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[11] Chinese Clinical Trial Registry. Available at: http://www.chictr.org.cn/searchproj.aspx?title=%E6%B0%AF%E5%9B%BD%E7%9A%84%E4%BF%9D%E5%85%B8%E7%A8%8B%E5%8F%AF%E8%AF%A2%E4%B8%8B%E9%92%9F%E7%BD%91&city=&institution=&institutionlevel=&measure=&intercode=&sourceofspends=&createyear=0&isuploadrf=&whetherpublic=&btngo=btn&verifycode=&page=1

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