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EDITORIAL

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

Mohamed F. Allam^{1,*}

¹Faculty of Medicine, Ain Shams University, Family Medicine, Cairo, Abbasia, Egypt

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 No attempts were made to locate any unpublished studies.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] *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.

References	Type of Study	Results
Expert consensus [4]	Expert consensus on the effectiveness of chloroquine for treatment of COVID-19 pneumonia.	Chloroquine improves outcome and shortens hospital stay.
Yao <i>et al.</i> [5]	<i>In vitro</i> Antiviral Activity of Hydroxychloroquine against Severe Acute Respiratory Syndrome COVID-19.	Hydroxychloroquine was found to be more potent than chloroquine to inhibit COVID-19.
Dong <i>et al.</i> [6]	Undergoing clinical studies to test the efficacy and safety in the treatment of COVID-19.	Tested drugs include chloroquine, arbidol, remdesivir, and favipiravir.
Touret and de Lamballerie [7]	Review and recommendations for the use of chloroquine in treating COVID-19. Information in light to previous experiments.	Chloroquine could be effective in treating COVID-19.
Gao <i>et al.</i> [8]	Multicenter clinical trials currently conducted in China to evaluate the efficacy of chloroquine in treating COVID-19 associated pneumonia.	Chloroquine has apparent efficacy and acceptable safety against COVID-19 associated pneumonia. Recommended to be included in the Guidelines.

(Table 3) contd....

References	Type of Study	Results
Colson <i>et al.</i> [9]	Review and recommendations. Usage of chloroquine in treating COVID-19.	Chloroquine could be used for treating COVID-19.
Wang <i>et al.</i> [10]	<i>in vitro</i> usage of remdesivir and chloroquine to inhibit COVID-19.	Remdesivir and chloroquine could inhibit COVID-19.

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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