Chloroquine in COVID-19: the evidence

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To the Editor

The Coronavirus disease 2019 (COVID-19) has been declared as a pandemic by World Health Organisation (WHO). The global mortality has increased, especially in countries like Italy and Iran. With the increasing morbidity and mortality, search for a cure has been the global demand. A recent randomized control trial has not found any benefit of lopinavir and ritonavir in clinical improvement and mortality [1]. Chloroquine has also been evaluated in individual studies and may have a role in the management of COVID-19 in the times to come [2]. The published literature till date has been summarised in the Table 1 below. The interim conclusions from the published literature is that there is no current evidence of use of chloroquine for treatment of COVID-19. The use should be restricted to clinical trials with strict vigilance and follow up to further clarify the role. As of date 23 clinical trials are underway [2], only after the results of which, can the role of chloroquine in management of COVID-19 be decided.

Table 1. Summary of trials/studies published on role of chloroquine in COVID-19.

Study	Patient	Intervention	Comparator	Outcome	Caveat
Letter to Editor [3]	>100 patients. Study done in China	Chloroquine, dose not mentioned	Not known	The statement reads as "treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course according to the news briefing." Thus, no specific primary or secondary end-points	No clinical details of any patient or outcome mentioned for readers/reviewers to analyse
Letter to Editor [4]	*In vitro* study	Remdesivir and chloroquine	Not known	*In vitro* inhibition	*In vitro* data should not be extrapolated to human beings without being tested
Commentary [5]	Not applicable	Not applicable	Not applicable	Not applicable	Use to be evaluated with promising announcements and potential detrimental effects observed in previous attempt to treat viral illness
Expert consensus [6]	Age >18 years and <65 years. (1) Mild: clinical symptoms are mild, and no pneumonia manifestations on imaging. (2) Ordinary type: with fever, respiratory tract symptoms, etc., imaging shows pneumonia. (3) Heavy: Meet any of the following: i) Respiratory distress, breathing rate >30 times/min; ii) In resting state, means oxygen saturation <93%; iii) Arterial partial pressure of oxygen (PaO_2) / inhaled oxygen concentration (FiO_2) <300 mmHg (1 mmHg = 0.133kPa).	Chloroquine phosphate tablet, at a dose of 500 mg twice per day for 10 days	Not applicable	During the course of treatment, if the nucleic acid of the throat swab becomes negative and is negative for 3 days, the drug withdrawal can be considered, but the minimum course of treatment needs 5 days. DISCHARGE: When the body temperature has returned to normal for more than 3 days, the respiratory symptoms have improved significantly, pulmonary imaging has shown significant inflammation absorption, and two consecutive respiratory pathogen nucleic acid tests negative (sampling interval of at least 1day), can be released from hospital or transferred to the appropriate department for other diseases according to the condition.	Adverse reactions, drug interactions, frequent electrocardiogram, hemogram, ophthalmology monitoring and mental status changes. Antibiotics such as quinolones and macrolides are forbidden

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Table 1. Continued from previous page.

Study	Patient	Intervention	Comparator	Outcome	Caveat
Dutch CDC [7] **Currently, the document has been removed from the source**	Severe infections requiring admission to the hospital and oxygen therapy or admitted to the ICU	The suggested regimen in adults- 600 mg of chloroquine base followed by 300 mg after 12 h on day 1, then 300 mg/day on days 2-5 days	Not applicable	Not applicable	This document also underlined 1) the needs for stopping thetreatment at day 5 to reduce the side effects, considering the long half-life (30 hours); 2) the need to differentiate betweenchloroquine phosphate and chloroquine base since 500 mg of the first correspond to 300 mg of the second
Italian Society of Infectious and Tropical Diseases [8] **The document is currently inaccessible**	Italian Society of Infectious and Tropical disease (Lombardy section)	Chloroquine 500 mg/day or hydroxychloroquine 200 mg for 10 days, although the treatment may vary from 5 to 20 days according to clinical severity	The document is currently inaccessible	The document is currently inaccessible	The document is currently inaccessible
France [9]	Open label non-randomized clinical trial	Confirmed COVID-19 in a single arm protocol from early March to March 16th, to receive 600 mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on their clinical presentation, azithromycin was added to the treatment	Untreated patients from another center and cases refusing the protocol were included as negative controls. **Presence and absence of virus at Day 6-post inclusion was considered the end point**	Viral load concentration was the end point. However, no mention of clinical outcomes mentioned	No clinical rationale of when and why did they decide the azithromycin to be added. Also, if the supplementary table is analysed the patients on chloroquine event showed increase in viral load on the contrary

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