LETTER TO THE EDITOR

USE OF CHLOROQUINE OR HYDROXYCHLOROQUINE IN TREATMENT OF COVID-19: IS IT ETHICAL?

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Since the Chinese health authorities declared the novel coronavirus (COVID-19) outbreak last December, 2019, several diagnosis and treatment protocols were published. Chloroquine, a known antimalarial drug, was suggested among the pilot treatments for COVID-19 (1).

A comprehensive search in PubMed from July 1966 to 1 January 2020 identified 20 publications about coronaviruses and chloroquine. Of which, 16 publications were in-vitro and in-vitro experiments and 4 were narrative reviews. The identified studies were published between 1987 and 2019. None of the recent recommendations to treat COVID-19 with chloroquine were based on randomized controlled clinical trials (RCTs). Also, the recommendations included various doses and regimens; some of which combined chloroquine or its metabolite, hydroxychloroquine, with other drugs such as azithromycin (1, 2).

Last April 2020, a report of the European Medicine Agency recommended chloroquine for treatment of COVID-19 only in RCTs or emergency use programmes (3). The politicization and premature use of chloroquine and hydroxychloroquine in the treatment of COVID-19 threatened the drug supply for patients who use it for chronic conditions such as systemic lupus erythematosus and rheumatoid arthritis (4, 5).

On 27 April 2020, Juurlink outlined the potential hazards associated with the use of chloroquine and hydroxychloroquine with azithromycin in the management of COVID-19 (6). Studies have shown that the combination of chloroquine or hydroxychloroquine with azithromycin increases the risk of QT prolongation and possibly increases mortality in COVID-19 patients (7–9). Concurrently, in the same month in Sweden, several hospitals stopped using chloroquine for treating COVID-19 after reports of several severe side effects (10).

Factors such as small sample size, lack of a control group, baseline differences between control and intervention groups and variation in drug dosage and regimens conflict the efficacy of chloroquine (11, 12). Despite some reported reduction in viral load and viral RNA clearance time, no trials have proven that chloroquine or its metabolites have significant clinical benefits such as reduction in morbidity, mortality and hospital stay associated with COVID-19 (9, 11, 13–15).

Most recently, the UK's Recovery Trial, the largest trial, revealed that hydroxychloroquine is not effective in the treatment of hospitalized COVID-19 patients and does not reduce mortality or morbidity (9, 11). On 15 June 2020, the US Food and Drug Administration (FDA) revoked the authorization for hydroxychloroquine and chloroquine emergency use, which was previously granted to the Strategic National Stockpile to treat a subset of hospitalized COVID-19 cases (16). The World Health Organization (WHO) temporarily stopped the hydroxychloroquine arm in the Solidarity trial, then later resumed it. Similarly, in the UK's large Recovery Trial the safety board noted no sign of harm to participants. The current knowledge on COVID-19 is fluent (11).

Undoubtedly, Phase II and III RCTs are needed to assess the efficacy and adverse events of the use of chloroquine or hydroxychloroquine in treating COVID-19 (17).

To date, the use of chloroquine or hydroxychloroquine in COVID-19 treatment is restricted to clinical trials. The efficacy of chloroquine or hydroxychloroquine in pre- or post-exposure prophylaxis groups is unknown and pending the outcomes of clinical trials.

This raises the following questions: is the current use of chloroquine or hydroxychloroquine, while awaiting RCTs results, ethical? Should the medical community hold off its use while the RCT results pend? Is it ethical to suggest the prophylactic use of chloroquine or hydroxychloroquine for healthcare workers?

Conflicts of Interests
None declared

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