First evaluation of hydroxychloroquine recommendations in treating SARS-CoV-2

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an infection caused by coronavirus disease 2019 (COVID-19), a novel virus for which no antiviral treatment was known when it first emerged. Since the publication of the first results from China on the use of chloroquine and its derivatives *in vitro* [1] and *in vivo* [2], followed by the publication of the results of a trial in Marseille on the combined use of hydroxychloroquine and azithromycin [3], many countries have adopted this treatment to treat patients with SARS-CoV-2. Over 60% of humans worldwide live in a country where chloroquine and its derivatives are recommended to treat patients with SARS-CoV-2. Other countries, awaiting the results of clinical trials to define their strategy or worried about potential adverse effects that have not yet manifested, have favoured other treatments or preferred the standard of care. This has not stopped physicians from turning *en masse* to hydroxychloroquine as a treatment for SARS-CoV-2, as shown by the results of surveys conducted by Sermo during spring 2020 [4].

Today, now that the epidemic is in a phase of decline in most of the hardest-hit countries in terms of mortality [5], we can issue initial assessments of the treatment strategies adopted in the world according to mortality in each country. We therefore determined which countries recommended hydroxychloroquine using the recommendations issued by the authorities of these countries, using data collected by c19study.com (Fig. 1). We then created a map classifying countries according to how they were affected by the epidemic (in number of deaths per million inhabitants) using data gathered by Worldometers.info (Fig. 2).

A comparison of these two maps shows that developing countries have turned *en masse* to the use of hydroxychloroquine, as have Asian countries, which have low mortality due to SARS-CoV-2 even though they were the first to be affected by the epidemic. These countries have in common the early adoption of treatments based on hydroxychloroquine and chloroquine, sometimes in combination with other antivirals. The countries which have expressed concerns regarding its use



FIG. 1. Countries using and countries limiting hydroxychloroquine in treatment of patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Grey indicates no information or unclear guidelines. Source: c19study.com (https://c19study.com/).



FIG. 2. Countries sorted by mortality per million inhabitants. Source: Worldometer (https://www.worldometers.info/coronavirus/).

are mainly rich countries (France, Germany, United States). It should be noted that Chinese studies show that China has adopted aggressive strategies against the virus in its treatment protocols, often combining up to three antivirals [6]. This therefore shows a discrepancy between the strategies of the Western world and those of developing countries and the Far East, with some countries being much more cautious than others regarding treatment provision to fight the epidemic. The opposite distribution of chloroquine recommendations and fatality rates is striking and must be investigated more deeply.

Conflict of interest

None declared.

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References

- [I] Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 2020;30:269–71.
- [2] Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends 2020;14:72-3.
- [3] Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents 2020;56:105949.
- [4] Sermo. COVID-19 trend reports: COVID-19 real time barometer data. Available at. 2020. https://app.sermo.com/covid19-barometer.
- [5] Coronavirus Resource Center; Johns Hopkins University. New cases of COVID-19 in world countries. Have countries flattened the curve? Updated. Available at:. 7 June 2020. https://coronavirus.jhu.edu/data/ new-cases.
- [6] Chen J, Liu D, Lui L, Liu P, Xu Q, Xia L, et al. [A pilot study of hydroxychloroquine in treatment of patients with moderate COVID-19]. Zhejiang Da Xue Xue Bao Yi Xue Ban 2020;49:215–9.