Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

Hydroxychloroquine/ chloroquine as a treatment choice or prophylaxis for Covid-19 at the primary care level in developing countries: A *Primum non Nocere* dilemma

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ABSTRACT

The Food and Drug Administration (FDA) warned against the use of Hydroxychloroquine or chloroquine for Covid-19 outside of a hospital or a clinical trial setting due to the risk of QT interval prolongation, ventricular tachycardia and the increased risk of these complications when combined with some antibiotics such as azithromycin. Several studies have reported no benefit of Hydroxychloroquine or chloroquine, when used alone or with a macrolide in COVID-19 hospitalized patients.

Despite these warnings, in several developing countries the official guidelines for treatment of Covid-19 patients at the primary care level recommend Hydroxychloroquine and azithromycin, among other treatments, as the first-choice for mild symptomatic Covid-19 patients, asymptomatic contacts or for prophylaxis. In our opinion there is a primum non nocere dilemma during this Covid-19 pandemic. In order to solve this bioethical problem, we strongly recommend that a randomized controlled trial in a primary care setting be carried out as a matter of urgency in these areas of the world.

In March 2020 hydroxychloroquine (HC) was reported to have a positive effect in a Covid-19 treatment open-label non-randomized clinical trial [1]. However, in recent Covid-19 observational studies in hospitalized patients, HC was not associated with a reduction in mortality, either alone [2] or in combination with azithromycin [3] and the need for randomized, controlled trials was recommended [2].

On April 21st 2020, a panel of the United States National Institutes of Health (NIH) recommended that no agent should be used for the treatment of SARS-CoV-2 outside the setting of a clinical trial. At that time no drug had been proven to be safe and effective for treating Covid-19 [4] although, Beigel et al. have recently reported that remdesivir does accelerate recovery from advanced Covid-19 [5]. On April 30th 2020, the Food and Drug Administration (FDA) also warned against the use of HC or chloroquine for Covid-19 outside of a hospital or a clinical trial setting due to the risk of QT interval prolongation, ventricular tachycardia and the increased risk of these complications when combined with some antibiotics such as azithromycin [6].

The World Health Organization (WHO) launched an international clinical trial, “Solidarity”, looking for an effective treatment for Covid-19, comparing four treatment options (including HC) against standard of care in hospitalized patients [7]; however, on May 24th, WHO decided to suspend temporarily the HC arm within the trial [8].

Despite these warnings, in several developing countries the official guidelines for treatment of Covid-19 patients at the primary care level recommend HC and azithromycin, among other treatments, as the first-choice for mild symptomatic Covid-19 patients, asymptomatic contacts or for prophylaxis [9,10]. There are several ethical concerns about this recommendation: 1) Lack of scientific evidence; 2) Increased risk of adverse events, especially cardiac complications; 3) Limited resources to evaluate complications in primary care (e.g, ECG equipment), 4) No consent form required in these guidelines; and 5) Educational issues specific to developing countries.

In our opinion there is a *primum non nocere* dilemma during this Covid-19 pandemic. In order to solve this bioethical problem, we strongly recommend that a randomized controlled trial in a primary care setting be carried out as a matter of urgency in these areas of the world.

References

[1] P. Gautret, J.C. Lagier, P. Parola, et al., Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial, Int. J. Antimicrob. Agents (Mar 20, 2020) 105949, https://doi.org/10.1016/j.ijantimicag.2020.105949.

[2] J. Geleris, Y. Sun, J. Platt, et al., Observational study of hydroxychloroquine in hospitalized patients with covid-19, Engl. J. Med. (May 7, 2020), https://doi.org/10.1056/NEJMoa2012410 (Online ahead of print).

[3] E.S. Rosenberg, E.M. Dufort, T. Udo, et al., Association of treatment with hydroxychloroquine or azithromycin with in-hospital mortality in patients with COVID-19 in New York State, JAMA (May 11, 2020), https://doi.org/10.1001/jama.2020.8630 (Online ahead of print).

[4] https://www.covid19treatmentguidelines.nih.gov/overview/ accessed in May 28, 2020.

[5] J.H. Beigel, K.M. Tomashek, L.E. Dodd, et al., Remdesivir for the treatment of covid-19 - preliminary report, N. Engl. J. Med. (May 22, 2020), https://doi.org/10.1056/NEJMoa2007764 Online ahead of print.

[6] https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or accessed in May 28th, 2020.

https://doi.org/10.1016/j.jns.2020.116972
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0022-510X/

[7] https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments accessed in May 28th, 2020.
[8] https://www.who.int/news-room/q-a-detail/q-a-hydroxychloroquine-and-covid-19 accessed in May 28th, 2020.
[9] http://www.salud.gob.hn/site/index.php/component/edocman/etapas-manejo accessed in May 28th, 2020.
[10] A. Kapoor, U. Pandurangi, V. Arora, et al., Cardiovascular risks of hydroxychloroquine in treatment and prophylaxis of COVID-19 patients: a scientific statement from the Indian Heart Rhythm Society, Indian Pacing Electrophysiol. J. 20 (3) (May–Jun, 2020) 117–120, https://doi.org/10.1016/j.ipej.2020.04.003 (Epub 2020 Apr 8).

Marco T. Medina[a,*], Sir Salvador Moncada[b]
[a] *Faculty of Medical Sciences, National Autonomous University of Honduras, WFN Regional Director for Latin America, Tegucigalpa, Honduras*
[b] *Manchester Cancer Research Centre, The University of Manchester, Manchester, UK*
E-mail addresses: marcotmedina@yahoo.com, marco.medina@unah.edu.hn (M.T. Medina).

* Corresponding author.