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.

Clinical Microbiology and Infection 27 (2021) 134–135

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Letter to the Editor

Re: 'Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients' by Fiolet *et al.*

Alexis Lacout [1, *], Pierre Yves Marcy [2], Christian Perronne [3]

[1)] *Centre de Diagnostic, ELSAN, Centre Médico–Chirurgical, 83 avenue Charles de Gaulle, 15000 Aurillac, France*
[2)] *Radiodiagnostics and Interventional Radiology Department, ELSAN, Polyclinique Les Fleurs, Quartier Quiez, 83190 Ollioules, France*
[3)] *Infectious Diseases Unit, University Hospital Raymond Poincaré, APHP Versailles Saint Quentin University Garches, France*

ARTICLE INFO

Article history:
Received 30 August 2020
Received in revised form
6 September 2020
Accepted 15 September 2020
Available online 25 September 2020

Editor: L. Leibovici

To the Editor,

We read with interest the paper by Fiolet *et al.* entitled "*Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients: a systematic review and meta-analysis*" recently published in Clinical Microbiology and Infection 2020 [1].

Further to this article we performed an extensive literature review and found many other studies dealing with the same topic that were published in good-quality peer-reviewed journals. But regrettably these were not considered by the authors despite their having performed (as they stated) an extensive research of the literature, as mentioned in their 'Material and methods' section [1].

The essence of a systematic review is that it should take into account all the data in order to make a rigorous, open and fair-minded synthesis on the topic. At least three meaningful studies that met the inclusion/exclusion criteria and were in favour of the efficacy of hydroxychloroquine and azithromycin in COVID-19 patients were discarded [2–4]. This approach is more akin to cherry-picking than to a true systematic review without *a priori* considerations.

Furthermore, the authors acknowledge in their article that only one study included non-hospitalized outpatients. Fiolet *et al.* stated: "*Despite our inclusion criteria that did not specify the stage of the disease, all the studies were conducted with hospitalized patients except the RCT by Skipper et al.*" [1]. In Skipper's study, although the difference was not statistically significant due to the small number of patients included [5], there were twice as many hospitalized patients in the placebo group (four hospitalizations out of 231 patients with hydroxychloroquine versus ten hospitalizations out of 234 patients with placebo). Last but not least, only 34% of those patients received appropriate PCR testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which adds to the confusion.

Heart rhythm disorders might be prevented in the hospital environment by monitoring with ECG and serum potassium measurement. The 'recovery' study did not meet the inclusion criteria as non-PCR-tested patients were included [6]. In addition, the doses of hydroxychloroquine given to COVID-19 patients in this study (2400 mg on the first day, followed by 9 days at 800 mg/day) were high and thus potentially toxic.

We are awaiting appropriate clinical trials or a thorough systematic review and meta-analysis to close the French and worldwide debate on whether treating patients with hydroxychloroquine/azithromycin in the early phase of COVID-19 infection improves their outcome.

Author contributions

AL: conceptualization, writing original draft. PYM: writing, review and editing. CP: supervision.

Transparency declaration

The authors have no conflicts of interest to disclose. No external funding was received.

References

[1] Fiolet T, Guihur A, Rebeaud M, Mulot M, Peiffer-Smadja N, Mahamat-Saleh Y. Effect of hydroxychloroquine with or without azithromycin on the mortality of COVID-19 patients: a systematic review and meta-analysis. Clin Microbiol Infect 2020. https://doi.org/10.1016/j.cmi.2020.08.022.

DOI of original article: https://doi.org/10.1016/j.cmi.2020.08.022.
* Corresponding author: Alexis Lacout, Centre de diagnostic, ELSAN, Centre médico–chirurgical, 83 avenue Charles de Gaulle, 15000 Aurillac, France.
E-mail address: lacout.alexis@wanadoo.fr (A. Lacout).

https://doi.org/10.1016/j.cmi.2020.09.027
1198-743X/

[2] Davido B, Boussaid G, Vaugier I, Lansaman T, Bouchand F, Lawrence C, et al. Impact of medical care including anti-infective agents use on the prognosis of COVID-19 hospitalized patients over time. Int J Antimicrob Agents 2020;56. https://doi.org/10.1016/j.ijantimicag.2020.106129 (published online ahead of print, 2020 Aug 2).
[3] Castelnuovo A, Costanzo S, Antinori A, Berselli N, Blandi L, Bruno R, et al. Use of hydroxychloroquine in hospitalised COVID-19 patients is associated with reduced mortality: findings from the observational multicentre Italian CORIST study. Eur J Intern Med 2020. https://doi.org/10.1016/j.ejim.2020.08.019. S0953-6205(20)30335-30336.
[4] Catteau L, Dauby N, Montourcy M, Bottieau E, Hautekiet J, Goetghebeur E, et al. Low-dose hydroxychloroquine therapy and mortality in hospitalized patients with COVID-19: a nationwide observational study of 8075 participants. Int J Antimicrob Agents 2020:106144. https://doi.org/10.1016/j.ijantimicag.2020.106144 (published online ahead of print 2020 Aug 24).
[5] Skipper CP, Pastick KA, Engen NW, Bangdiwala AS, Abassi M, Lofgren SM, et al. Hydroxychloroquine in nonhospitalized adults with early COVID-19: a randomized trial. Ann Intern Med 2020. https://doi.org/10.7326/M20-4207. M20-4207 (published online ahead of print, 2020 Jul 16).
[6] Horby P, Mafham M, Linsell L, Bell JL, Staplin N, Emberson jr, et al. Effect of hydroxychloroquine in hospitalized patients with COVID-19: preliminary results from a multi-centre, randomized, controlled trial. MedRxiv 2020;2020. https://doi.org/10.1101/2020.07.15.20151852. 07.15.20151852.