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.

Travel Medicine and Infectious Disease 37 (2020) 101826

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Correspondence

Apparent inefficacy of hydroxychloroquine combined with azithromycin on SARS-CoV-2 clearance in an incident cohort of geriatric patients with COVID-19

To the Editor:

Gautret at al. published results of non-randomized studies suggesting efficacy of hydroxychloroquine and azithromycin (HCQ/AZI) in patients with COVID-19 [1,2]. Particularly, among 80 mildly infected patients, 83% at day 7 and 93% at day 8 achieved negative results of RT-PCR for SARS-CoV-2 from nasopharyngeal swabs [2]. More recently, data from a multicenter study of 1061 patients were published, showing that all but one patient were PCR-cleared at day 15 [3].

Following the extraordinary success rate of the first study [1], we started prescribing HCQ/AZI in our patients, so from March 28th to April 4th, 2020, 41 patients took HCQ (200 mg thrice daily) and AZI 500 mg for the first day and 250 mg for the subsequent 4 days. All patients got infected from a unique outbreak in a long-term facility, with the date of infection estimated around a week before admission. So, in this study on an incident cohort, we minimized the risk of interpreting a rapid PCR clearance as an effect of the prescribed treatment, while such clearance may be simply spontaneous in patients infected for a longer time.

Among 41 patients, ten died for severe COVID-19 (6 patients took treatment for $\leq$2 days, and 4 for $<$5 days), and one refused to be retested for SARS-CoV-2. So, 30 patients were evaluated after completion of the treatment course. Among them, 17 (51%) were females; median age was 83 years (IQR: 65–88). Recorded comorbidities were: hypertension (76.6%), neurological diseases (43.3%), chronic kidney disease (43.3%), and psychiatric disorders (33.3%). Nine (30%) patients were diagnosed with COVID-19 pneumonia (three requiring oxygen support). Twelve patients had upper respiratory symptoms. Five patients had respiratory failure without radiological evidence of pneumonia. Four patients were asymptomatic. Real time reverse transcriptase–polymerase chain reaction (RT-PCR) to detect SARS-CoV-2 genome on nasopharyngeal swabs was performed with Gene Finder TM COVID-19 Plus RealAmp Kit, ELITech Group, Puteaux, France.

After one week from starting treatment, only 3 (10%) patients reported negative results on nasopharyngeal swabs. All the other patients remained positive also at the following swab after one week. Twenty-nine patients survived and became asymptomatic, but one 84 year-old man remained positive and died three weeks after treatment.

In conclusion HCQ in combination with AZI did not show an effect comparable to that obtained in other studies [1–3]. Clearly, patient characteristics (age, comorbidities, more severe diseases) may have played a role in reducing the rate of virological response. However, since in our incident cohort patients were treated soon after the putative date of infection, the apparent discrepancy may also be due to selection of patients who needed more time to reach spontaneous clearance, while those treated by Gautret at al [2]. may have received HCQ and AZI closer to the moment when natural clearance of SARS-CoV-2 would have occurred anyway. This indicated both the importance of a careful selection of patients in non-randomized studies and the critical need of randomized trials to get a definitive answer as to whether or not HCT/AZI works in patients infected by SARS-CoV-2.

Ethics approval and consent to participate

Ethical approval of the protocol was obtained and consent for participation was obtained from each patients.

Availability of data and materials

All data and materials used in this work were publicly available.

Funding

This work was not funded.

Disclaimer

The funding agencies had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Authors' contributions

All authors conceived the study, carried out the analysis, discussed the results, drafted the first manuscript, revised the manuscript, and gave final approval for publication.

Declaration of competing interest

The authors declared no competing interests.

Acknowledgements

We want to thank all our patients and our nurses. We also thank the Infectious Diseases and Tropical Medicine (IDTM) of the University "Magna Graecia" (UMG) COVID-19 Group, which is composed, besides the main authors, by the following: Eugenio Arrighi, Giorgio Settimo Barreca, Flavia Biamonte, Bernardo Bertucci, Maria Teresa Busceti, Anna Cancelliere, Francesco Saverio Costanzo, Luigia Gallo, Aida Giancotti, Amerigo Giudice, Angelo Lamberti, Maria Carla Liberto, Elena Lio, Rosaria Lionello, Nadia Marascio, Giuseppina Marrazzo, Giovanni Matera, Maria Chiara Pelle, Maria Petullà, Graziella Perri, Giada Procopio, Angela Quirino, Marco Ricchio, Francesca Serapide,

https://doi.org/10.1016/j.tmaid.2020.101826
Received 14 May 2020; Accepted 27 July 2020
Available online 31 July 2020

Bruno Tassone.

References

[1] Gautret P, Lagier J-C, 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. https://doi.org/10.1016/j.ijantimicag.2020.105949.

[2] Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Sevestre J, et al. Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: a pilot observational study. Trav Med Infect Dis 2020. https://doi.org/10.1016/j.tmaid.2020.101663.

[3] Million M, Lagier JC, Gautret P, Colson P, Fournier PE, Amrane S, Hocquart M, Mailhe M, Esteves-Vieira V, Doudier B, Aubry C, Correard F, Giraud-Gatineau A, Roussel Y, Berenger C, Cassir N, Seng P, Zandotti C, Dhiver C, Ravaux I, Tomei RD. Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: a retrospective analysis of 1061 cases in marseille, France. Trav Med Infect Dis 2020. https://doi.org/10.1016/j.tmaid.2020.101738.

Maria Mazzitelli[a,*], Chiara Davoli[a], Vincenzo Scaglione[a], Paolo Fusco[a], Valentina La Gamba[a], Giovanni Matera[b], Enrico Maria Trecarichi[a], Carlo Torti[a]

[a] *Infectious and Tropical Disease Unit, Department of Medical and Surgical Sciences, Magna Graecia University of Catanzaro, Italy*

[b] *Clinical Microbiology Unit, Department of Health Sciences, Magna Graecia University of Catanzaro, Italy*

[*] Corresponding author. Infectious and Tropical Disease Unit, "Magna Graecia" University, Viale Europa, 88100, Catanzaro, Italy.
E-mail address: m.mazzitelli88@gmail.com (M. Mazzitelli).