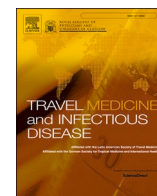




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Correspondence



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 et 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 ≤ 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 et 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.

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Disclaimer

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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.

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