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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Letter to the Editor

Focus on clinical outcomes of "Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial"

To the Editor: I've have read with great interest the therapeutic article by Gautret et al. [1] which showed increased clearing of SARS-CoV-2 by RT-PCR from the nasopharyngeal samples taken until the 6th day of their patients. The article immediately circulated throughout the world with the new hope of an accessible therapy with low dose azithromycin combined with high dose hydroxychloroquine.

However, the clinical outcomes are the pivotal aspect of therapeutics. Since the goal is to treat people, not viruses, a positive viral swab not necessarily means a person is infected: asymptomatic carriers are observed to have become negative as soon as the next day (D1). A patient who is healing perfectly may still present a positive viral RNA test, which could be interpreted as a residual clearance positive test.

Considering the clinical outcomes presented, the hydroxychloroquine group did not perform better than the control arm, according to the severe adverse events reported: one patient presented severe nausea to the point of stopping therapy, 3 patients were admitted to the intensive care unit (over 10%), and 1 patient died (despite a negative viral test).

Although the control group in the reported 6 days had more favorable clinical outcome, there is great hope with azithromycin, which was still not reported as monotherapy, and the authors omitted to state if any of the excluded patients (due to severe adverse events) were taking specifically the combination.

More emphasis should have been given to the risk of torsades de pointes and sudden death by combining two drugs that prolong the QT interval, since acknowledging the risk, even if theorical, will only protect the patients by close monitoring. This duet could be inadvertently combined with a third because of nausea, and the trio could be fatal at any age. Extreme caution is advised in case the combination is used in admitted patients: continuous ECG monitoring with attention to the rhythm and the rate-corrected QT interval (QTc). Review medications immediately in case QTcF (Fridericia calculation) is approaching 500ms.

Strict avoidance of other medications that prolong QTc is advisable by checking a free online databank such as CredibleMeds [2]. And finally, because magnesium deficiency may be a triggering mechanism for torsades de pointes, magnesium supplementation may prevent life-threatening arrhythmias [3].

References

[1] 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 Jul 2020;56(1):105949.
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