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## Letter to the Editor

**Hydroxychloroquine (HCQ): real treatment or false hope?**

In the last few weeks the news about chloroquine (CQ) and Hydroxychloroquine (HCQ) gave the world populations the hope to cure the COVID-19, the disease caused by SARS cov-2 and led at the time of writing this commentary to 876,348 confirmed cases, 184,965 total recovered and 43,522 deaths [1].

Many clinical trials were conducted and are still running mainly in China: (ChiCTR2000029939, ChiCTR2000029935, ChiCTR2000029899, ChiCTR2000029898, ChiCTR2000029868, ChiCTR2000029837, ChiCTR2000029826, ChiCTR2000029803, ChiCTR2000029762, ChiCTR2000029761, ChiCTR2000029760, ChiCTR2000029740, ChiCTR2000029609, ChiCTR2000029559, and ChiCTR2000029542) [2]. some of them were canceled by the investigator. So far, we could not find any published results of such studies.

In France, a “quick” clinical trial evaluating the efficacy of HCQ and a combination of HCQ / Azithromycin in treatment of COVID-19 was released recently [3] pushing many countries to take decision to include these drugs in their strategies to treat COVID-19 patients. Consequently, many companies started already to produce and to make stocks of HCQ! Is it a wise decision?

Therefore, I want to draw your attention to some points of this study. From my point of view, the study was conducted, written and wrapped in one fell swoop and it needs to be reconsidered. Thus, any results from this study must be treated with caution before taking any decision at the international level.

The authors claimed in their study to evaluate the role of hydroxychloroquine on respiratory viral loads. Whereas the study is based only on the Cycle Threshold (CT) values of qRT-PCR. The CT values should be interpreted as number of copies/ml to have viral load or at least deltaCT values should be reported based on CT value reference. Also, the patients with CT values lower than 35 (cut off value) was considered at positive without any explanation of the choice of this value.

Even the study is not randomized, since the sample size is small the patients should be chosen according to similar/comparable criteria:

**Control group:** Only 6 out of 16 had CT values reported, what about the others and how they were considered as positive? For those without PCR results at D6 (ND), are they considered as positive or negative? But it seems that they have been considered as positive (fig 1 and Fig 2 [3])

**Treated groups:**

**HCQ group:** 14 patients with CT values ranged from 15 – 34 at D0, in 5 patients with high CT we can assume that the inefficacy of HCQ was due to the high viral load that was difficult to clear!

In addition to that, the time between the onset of the symptoms and the inclusion should be in reasonable range. In the HCQ treated group, it ranges from day 1 to day 10 after the onset of the symptoms which could really affect the result, for example: Patients 22, and 27 had high CT values, meaning they might have started to clear the virus, and the effect might be due to their immune system not to the treatment.

**HCQ + Azithromycin group:** This group is more homogenous compared to the previous one based on the time between the onset of symptoms and the inclusion, which is ranged from 2 to 7 days and also the CT values ranged from 23 to 30. The CT values are higher compared to HCQ group, meaning the viral loads are very low in these patients (even if it was not calculated). Hence, the clearance of the virus in this group might be due to the immune system or to the sole effect of HCQ or Azithromycin or combined action of the two?

Since the groups are not similar, the results could not be compared and any attempt to compare these groups is scientifically inadequate and may give false interpretation.

All treated patients should be followed up for a certain period of time without any treatment to see any other manifestations or relapse, before any final conclusion.

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**Ethical Approval:** N/A

**References**

- [1] <https://www.worldometers.info/coronavirus/>
- [2] Chinese Clinical Trial Registry. <http://www.chictr.org.cn>
- [3] 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* 2020;56(1):105949.

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