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Letter to the Editor

Effect estimation of hydroxychloroquine for COVID-19: a secondary analysis of an open label non-randomized clinical trial


Sir,

There is evidence that zinc ionophores, such as hydroxychloroquine, block the replication of coronaviruses in cell cultures. Recently, an open-label non-randomized clinical trial was published to propose a synergistic effect of hydroxychloroquine in combination with azithromycin to cure infection and treating transmission of SARS-CoV-2 in patients with COVID-19 [1].

The sample population for this study according to previously defined inclusion and exclusion criteria was selected from hospitalized patients in a healthcare facility located in Marseille, France. Only people that tested positive RT-PCR for SARS-CoV-2 from nasopharyngeal samples were included and followed for 14 days. Treatment arm was compared to supportive care. The primary endpoint was defined as the proportion of negative RT-PCR at day 6 post inclusion. Secondary aims were defined to describe changes in viral load over time, clinical course and side effects. To test for statistically significant differences between the two groups, depending on the nature of the variables, Pearson's chi-square test or Fisher's exact test, and Student's t-test were performed. Results showed significant differences between the two groups regarding the primary endpoint, where 70% of patients in the hydroxychloroquine group tested negative for RT-PCR at day 6 and only 12.5% patients did so in the control group ($p=0.001$). Using the clinical trial's data, Lover estimated the magnitude of the effect by performing a Cox proportional hazards model, finding that the impact of the intervention is low. The estimated HR was 3.026 (95% CI=0.925-9.895; $p=0.067$) for hydroxychloroquine users and for those who received hydroxychloroquine plus azithromycin an HR was 7.073 (95% CI = 1.722-29.044; $p = 0.007$) [2].

However, these two studies do not report some estimate measures of effect modification such as absolute risk reduction (ARR), relative risk reduction (RRR), and number needed to treat (NNT) [3], with the intervention of hydroxychloroquine. Considering the relevance of the results of this study regarding the problem of the COVID-19 pandemic, the need to make these estimations was raised for them to be considered by decision-makers. The analyzes were carried out using the STATA statistical package.

Table 1 shows the contingency table that was used to estimate the effect measures. The incidence of the chloroquine exposed

Table 1

Hydroxychloroquine and COVID-16 negative PCR: an open non-randomized clinical trial of 26 patients with chloroquine and 16 patients without chloroquine (6 cases excluded for the final analysis).

| | Event (negative PCR) | No event (positive PCR) |
|-------------------|----------------------|-------------------------|
| Case (HCQ) | 14 | 6 |
| Control | 5 | 11 |

group was 0.7 and the incidence of the unexposed was 0.3125%. The RRR was 1.24, the RAR was 0.3875 CI 95% (0.0843-0.6907) and NNT was 2.5806 CI 95% (1.4478-11.8594). According to the previously mentioned findings, it can be interpreted that by treating ~3 patients with hydroxychloroquine, the result of a positive PCR for COVID-19 can be decreased in one case. However, its wide confidence interval is striking.

Although being an open-label non-randomized clinical trial, is subject to multiple selection and information biases, these findings are a starting point and a light for the COVID-19 pandemic that to date affects 180 countries and who has claimed the lives of more than 42,139 people worldwide. More randomized studies are required to establish more robust results soon.

Declaration of Competing Interest

None

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Ethical Approval

Not required

References

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