Title: Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial

Author(s): Wei Tang, Zhujun Cao, Mingfeng Han, Zhengyan Wang, Junwen Chen, Wenjin Sun, Yaojie Wu, Wei Xiao, Shengyong Liu, Erzhen Chen, Wei Chen, Xiongbiao Wang, Jiuyong Yang, Jun Lin, Qingxia Zhao, Youqin Yan, Zhibin Xie, Dan Li, Yaofeng Yang, Leshan Liu, Jieming Qu, Guang Ning, Guochao Shi, Qing Xie

Journal title: British Medical Journal (BMJ)

Date, issue, pages of publication: BMJ 2020; 369: m1849

Digital object identifier: 10.1136/bmj.m1849

Introduction
This study aimed to assess the impact of hydroxychloroquine in the treatment of SARS-CoV-2 infection. The primary outcome was viral clearance by 28 days judged by negative RT-PCR.

Design
It was a multicentre, randomised, parallel, open-label trial involving in-patients with COVID-19 in 3 provinces in China.

Methods
150 patients were randomised. 148 had no supplemental oxygen requirement and were classed as mild disease (without pneumonia) or moderate disease (with pneumonia). Hydroxychloroquine was administered for 2 weeks - 1200mg daily for three days then 800mg daily thereafter.

Results
109 patients achieved viral elimination before 28 days. The median time in the hydroxychloroquine group was 8 days vs. 7 days in control group. There was no statistical difference in the probability of conversion to negative within 28 days between groups.

Conclusions
The study did not show an improvement in viral clearance with the addition of hydroxychloroquine to standard care in mild to moderate COVID-19 disease.

Discussion
This study's impact is reduced by several limitations. It was not double-blind or placebo controlled introducing investigator and other biases. The target enrolment numbers were not met, there was a small sample size due to issues with recruitment of eligible patients and early termination of the study. From an Irish perspective the cohort studied is not the typical sub-set of patients treated in Irish hospitals with COVID-19. The studied sample was a median of 16 days post onset of symptoms and 99% of participants did not require supplemental oxygen. The trial did not address drug effect on disease course or mortality which are important markers in practice, particularly as the clinical significance of persistently detectable viral RNA in respiratory samples is currently unclear.1

Reflection
In the rapidly evolving and high profile debate surrounding hydroxychloroquine use in the treatment of COVID-19, this study begins to establish some clarity. The
administration of the drug initially gained traction in Irish hospitals during the onset of the COVID-19 pandemic, stemming from evidence of improved outcomes in observational studies and case series along with in-vitro experiments\(^2\). In the small non-randomised French study by Guatret et al published in March, hydroxychloroquine seemed to result in remarkable improvement.\(^3\) Subsequent larger observational studies by Maheva et al\(^4\) and Gerleis et al\(^5\) showed no benefit, and worsening outcomes with hydroxychloroquine use. This trial undoubtedly will have an impact on current practice as it further adds to the growing body of evidence that the risks outweigh the benefits in the use of hydroxychloroquine in SARS-CoV-2 infection. The study also highlights that we must be cautious in our eagerness to offer yet-unproven treatments which may cause harm. Especially to more vulnerable patients who have been disproportionately affected by this pandemic, who may not be able to understand the risks they face and in whose best interest we are charged to make decisions.

References


